THE JOURNAL OF UROLOGY

Manuscripts submitted for publication and communications concerning editorial matters should be sent to Dr. J. A. Campbell Colston, Brady Urological Institute, Johns Hopkins Hospital, Baltimore 5, U. S. A.

Reprints of articles will be furnished to contributors when ordered in advance. A table showing cost of reprints, with an order slip, is sent with proof.

The Journal of Urology is issued monthly. Two volumes are issued each year beginning in January and July.

Correspondence concerning business matters should be addressed to The Williams & Wilkins Company, Publishers of Scientific Books and Periodicals, Mount Royal and Guilford Avenues, Baltimore, U. S. A.

Subscription price: \$5.00 per volume. For countries outside the Postal Union (North and South America and Spain), add 50 cents per volume, for delivery.

Claims for copies lost in the mails must be received within 30 days (domestic) Changes of address must be received within two weeks of the date of issue.

New subscriptions and renewals are entered to begin with the first issue of the current volume. Should any issue of the current volume be out of print at the time the subscription order is received, the pro-rata value of such numbers will be credited to the next volume, and the renewal invoice therefore adjusted accordingly.

Subscriptions should be renewed promptly—To avoid a break in your series, subscriptions should be renewed promptly. The publishers cannot guarantee to supply back issues on belated renewals.

Subscriptions, new or renewal, should be sent to the Publishers or to Agents listed below.

Vol-61 No-1 - Jan. 1949

AGENTS

For Australia: Angus & Robertson, Limited, 89-95 Castlereagh Street, Sydney.

For the British Empire, except Australia and Canada: Baillière, Tindall & Cox, 8 Henrietta St., Covent Garden, WC. 2, London, England.

For Canada: Wm. Dawson & Sons Ltd., 70 King Street East, Toronto.

PUBLISHED MONTHLY BY

THE WILLIAMS & WILKINS COMPANY

Publishers of Scientific Books and Periodicals

BALTIMORE-2, U. S. A.

MANDELAMINE

Urinary Antiseptic of Choice—*when therapy must be prolonged*—

MANDELAMINE

Reg U S Pat. Off

Cumulative clinical experience points up the numerous advantages of employing MANDELAMINE*—the chemical combination of methenamine and mandelic acid—in the management of urinary infections, especially when therapy must be prolonged, or repeated courses are indicated.

In contrast to the sulfonamides and streptomycin, administration of MANDELAMINE is not attended by the risk of drug-fastness,[1] affords virtually complete freedom from toxic or other untoward reactions,[2,3] facilitates treatment through an uncomplicated regimen, and secures optimal patient-cooperation. Significantly, bacteria that have become resistant to sulfonamides or streptomycin continue to exhibit full susceptibility to the action of MANDELAMINE.

1. Scudi, J. V., and Duca, C J · J Urol. (to be published). 2. Carroll, G., and Allen, H. N.: J. Urol. 55: 674 (1946). 3. Merricks, J. W.: West Virginia M. J. 44: 157 (1948).

*MANDELAMINE is the registered trademark [illegible] rand of [illegible]

6 OUTSTANDING FEATURES

1 No gastric upset
2 No dietary or fluid regulation
3 No supplementary acidification (except when urea-splitting organisms occur)
4 Wide antibacterial range
5 No danger of drug-fastness
6 Simplicity of regimen—3 or 4 tablets, t.i.d.

NEPERA

NEPERA CHEMICAL CO., INC
Manufacturing Chemists

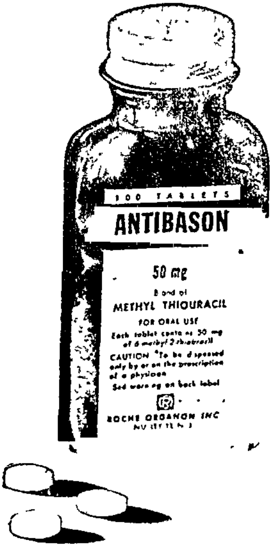
NEPERA PARK • YONKERS 2, N. Y.

A NEW ADVANCE

for the modern medical treatment of hyperthyroidism

Antibason (methyl thiouracil) 'Roche-Organon' culminates a long search for a highly potent thiouracil derivative which has minimal undesirable reactions. It has distinct advantages over other known thiouracil derivatives in the medical treatment of hyperthyroidism. Antibason provides prompt action, high efficacy, and minimal undesirable reactions; moreover, it may be used with gratifying results in cases refractory to other thiouracil compounds. For the average case of hyperthyroidism, a daily dose of 200 mg of Antibason will usually prove sufficient to control the symptoms, after which the dosage should be reduced to a maintenance level. Antibason is *available for physicians' prescriptions as 50-mg tablets in bottles of 100 and 1000. Descriptive literature on Antibason is available on request.*

ROCHE-ORGANON INC. • NUTLEY 10, NEW JERSEY



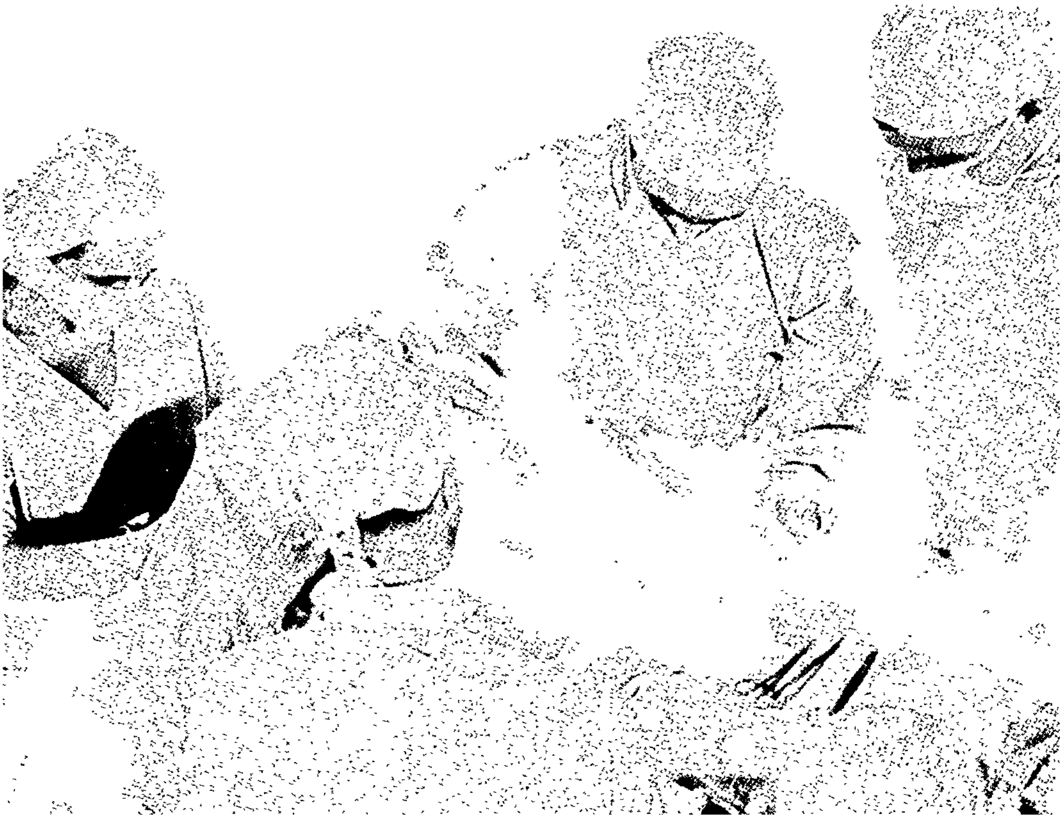
ANTIBASON (METHYL THIOURACIL)

T.M.—ANTIBASON—Reg. U.S. Pat. Off.

Dam the Blood WITH Hemo-pak

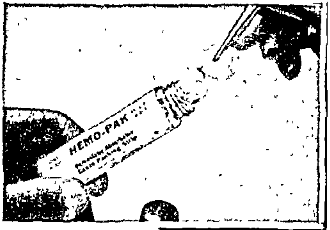
HEMO-PAK Hemostatic Absorbable Surgical Dressings consist of oxidized gauze or cotton in the form of sterile packing strips or cotton pads.

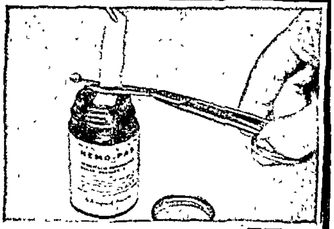
Just remove from the sterile, sealed tube . . . place in contact with the bleeding surface—with slight pressure. Within two minutes—like magic—the material turns black in contact with hemoglobin, forming an artificial clot to effectively dam bleeding vessels.

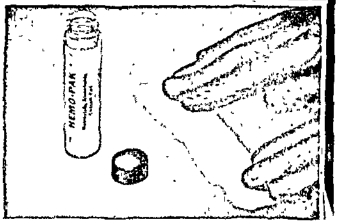


Hemo-Pak can be buried in most tissues with *safety* since—in a few days' time—absorption is complete, *with no ill effects nor local irritation.*

Hemo-Pak (Brand of Oxidized Cellulose) is a complete hemostatic unit, and, requiring no cumbersome manipulation, provides a prompt, effective, and practicable means of controlling hemorrhage even under the most inconvenient and difficult circumstances.







HEMO-PAK, [illegible] *types and three sizes:*

Hemostatic Absorbable Gauze Packing Strips:

(1) 2" x 14" for hemostasis in general surgery and where suturing or ligation is impractical or ineffective.

(2) ½" x 2½ yds. for postnasal packing following otolaryngologic procedures, and control of spontaneous hemorrhage.

Hemostatic Absorbable Cotton Pads:

(3) 6" x 2" for hemostasis in brain surgery. Each pad in sterile sealed tube or vial, packed 12 tubes to a box.

Johnson & Johnson

NEW BRUNSWICK, N. J.

Hemo-pak

Trade Mark

HEMOSTATIC ABSORBABLE SURGICAL DRESSINGS

KODACHROME
SLIDES
NOW
INCLUDING
GROSS
PATHOLOGY

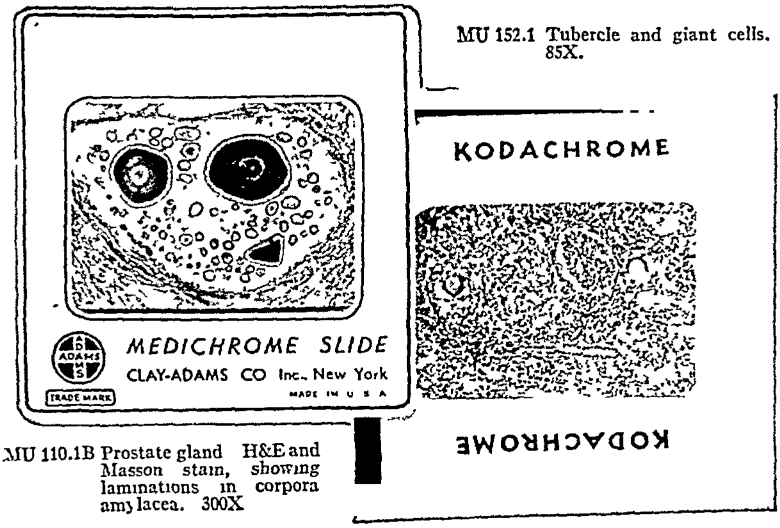
MUG/21 2 Clear cell carcinoma of kidney.

"MEDICHROME" SERIES MU UROGENITAL PATHOLOGY
Trade Mark Regd U. S. Pat. Off.

A series of 345 **photomicrographs** and **gross specimens**, made with the cooperation of **Dr. M. M. Melicow**, Department of Urology, College of Physicians and Surgeons, Columbia University.

"MEDICHROME" SERIES MU2 TESTICULAR BIOPSIES

A series of 49 photomicrographs made with the cooperation of **Dr. Samuel L. Siegler, Dr. Robert Sherman Hotchkiss, Dr. N. Chandler Foot** and **Dr. Maxwell J. Fein.** Syllabus covering the series, giving biopsy reports and complete case histories, available at $1.00.



MU 152.1 Tubercle and giant cells. 85X.

MU 110.1B Prostate gland H&E and Masson stain, showing laminations in corpora amylacea. 300X

PRICES

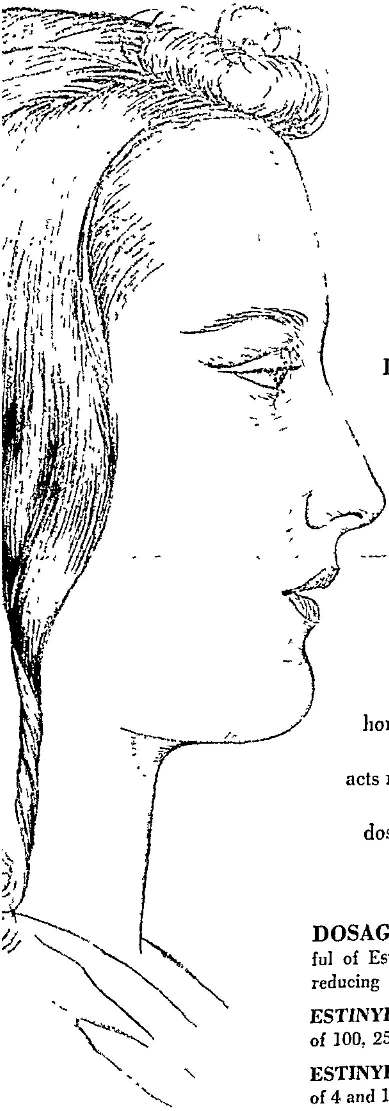
Bound between glass in Adams Slide Binders
$1.00 each

In cardboard readymounts
$.80 each

Less 5% for 50 slides, 10% for 100 or more slides

Write for complete listings on above MEDICHROMES

CLAY-ADAMS COMPANY, INC.
141 EAST 25th STREET · NEW YORK 10
Showrooms also at 308 West Washington Street, CHICAGO 8, ILL.



by far the most potent ORAL ESTROGEN available clinically

In exceedingly minute doses—as little as 0.02 mg. (1/3200 gr.) daily—ESTINYL* maintains the average menopausal patient free of symptoms. Even when initiating therapy and in the more severe cases, unusually small dosage—measured in hundredths of a milligram—has been found effective.

ESTINYL

(ETHINYL ESTRADIOL)

ESTINYL, a derivative of the ovarian follicular hormone, estradiol, evokes the sense of well-being characteristic of natural hormone therapy. It acts rapidly, often completely controlling climacteric symptoms within a few days. In therapeutic dosage side effects are notably infrequent. Unique response to minimal dosage permits effective estrogen therapy at low cost to patients.

DOSAGE: One ESTINYL Tablet (0.02 mg.) or one teaspoonful of ESTINYL LIQUID (0.03 mg.) daily, may be prescribed, reducing dosage as symptoms subside.

ESTINYL *Tablets, 0.02 (buff) or 0.05 mg. (pink), in bottles* of 100, 250 and 1000.

ESTINYL LIQUID, 0.03 mg. per 4 cc. (teaspoonful), in bottles of 4 and 16 oz.

*®

Schering CORPORATION · BLOOMFIELD, NEW JERSEY
IN CANADA, SCHERING CORPORATION LIMITED, MONTREAL

Announcing

Sterile

WHITE PETROLATUM

U.S.P.

BAYBANK BRAND

with the Break-tip tube-

This unbroken seal is your guaranty of sterility!

BAYBANK

Processed and packed under completely aseptic conditions, this new Baybank product can be relied upon at all times to be *thoroughly and dependably sterile!* Despite the rigorous sterilization process to which it is subjected, the Baybank brand of Sterile White Petrolatum U.S.P. retains all of the desirable properties of white petrolatum—with no change in color or development of odor, and with the same consistency, viscosity, and melting point.

For topical application—direct from handy collapsible tubes—to burns and wounds, (may be used in conjunction with 'VASELINE* Sterile Petrolatum Gauze Dressings); in packs, drains, protective coverings; or as a lubricant for gloves, catheters, and instruments in diagnostic and therapeutic procedures.

Exterior of tube may be sterilized by autoclaving for operating room use. Supplied in 1-oz collapsible tubes, packed 6 to a carton.

BAYBANK PHARMACEUTICALS, INC.
Division of Chesebrough Mfg. Co. Cons'd
17 STATE STREET • NEW YORK 4, N. Y.

*Trade-Mark

New Abstract Service

EXCERPTA MEDICA

Fifteen journals publishing pertinent and reliable abstracts in English of every article in every available medical journal

Journals cover Anatomy, Anthropology, Embryology and Histology; Physiology, Biochemistry and Pharmacology; Endocrinology; Hygiene and Medical Microbiology; General Pathology and Pathological Anatomy, and Bacteriology; Internal Medicine; Pediatrics; Neurology and Psychiatry; Surgery; Obstetrics and Gynecology; Oto-, Rhino-, Laryngology; Ophthalmology; Dermatology and Venereology; Radiology; and Tuberculosis.

Each journal is issued monthly, one or two volumes a year.

The Williams & Wilkins Company sole distributor for the United States, Canada and Central America.

Send for the free booklet giving complete information and descriptions of each journal

The Williams & Wilkins Company
Mt. Royal and Guilford Aves.
Baltimore 2, Md.

A DRUG HAS ACTION

and side-actions, too

The salicylates, for instance, "acidose" and the sulfa drugs may produce crystalluria.

The simultaneous administration of alkalies reduces these possibilities. It is effectively accomplished by prescribing

Kalak
(R)

A carbonated, polybase alkaline water

It is a zestful, refreshing, palatable drink which for years has distinguished itself as a therapeutic adjuvant of choice.

Available at all pharmacies

Kalak Water Co. of New York, Inc.
30 Rockefeller Plaza New York 20, N. Y.

criteria in syphilotherapy

"Therefore, more than in any other disease, it is necessary in the treatment of an individual patient with syphilis to follow a therapeutic regimen which, after *long term study* in *large series of patients*, has been established as *satisfactory* for the particular type of syphilis under consideration *

MAPHARSEN®

an arsenical of choice in the treatment of syphilis

long-term study

More than a decade of clinical evaluation

large series of patients

Over two hundred million injections already administered

satisfactory

High therapeutic effectiveness with notable safety in causing disappearance of spirochetes, healing of lesions and reversal of seropositivity in a large percentage of cases

MAPHARSEN (oxophenarsine hydrochloride P D & Co) is supplied in single dose ampoules of 0 04 Gm and 0 06 Gm , boxes of 10 and in multiple dose ampoules of 0 6 Gm in boxes of 10

*Cecil R A A Textbook of Medicine Philadelphia W B Saunders Co 1947 p 376

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN

PROMPT REPAIR SERVICE

Cutting Loops Expertly Rebuilt. Reasonable. Send us your burned Loops.

BAKELITE SHEATHS REPLACED

We manufacture and Repair all types of Electro-Surgical Electrodes & Accessories. Prices upon request.

GREENWALD CO., INC.
DEPT. E GARY, INDIANA

A book that is always welcome

because its message has remained true and alive through 2500 years.

THE GENUINE WORKS OF HIPPOCRATES

- In the classical translation of Francis Adams that preserves the spirit of the original.
- Edited to give a connected picture of medicine in the Golden Age of Greece.
- Printed and bound to make a beautiful volume of four hundred pages.

Here is medical observation at its keenest. There hardly exist more accurate word pictures of sick men, more careful descriptions of their appearances. The book in its present form, free from technical annotations of former editions, stands out more than ever as a great contribution to medicine and world literature.

"This true medical bible will interest, if not fascinate all students of medicine, both general and special."—N. Y. *State Journal of Medicine.*

Edited and introduced by Emerson Crosby Kelly

390 pages 8 plates $3.00

THE WILLIAMS & WILKINS CO.
Baltimore 2, Maryland

RADON

When interstitial radiation is indicated, the ALL GOLD radon implant is recommended.

Our Radon Implants are ALL GOLD—24 Karat—and excellent for intratumoral implantation.

High temperature sterilization is possible with utmost safety.

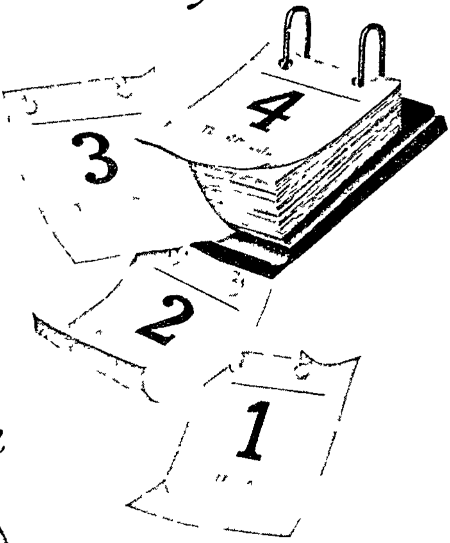
Accurate dosage is assured because the ALL GOLD radon implant is sold with a guarantee as to radon content at hour of use.

•

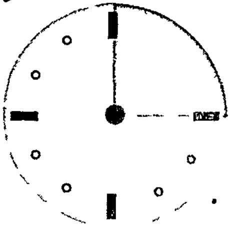
Prices and Literature on Request.

RADIUM CHEMICAL COMPANY • Inc.
570 Lexington Ave., New York, 22, N. Y.
Chicago: Marshall Field Annex Building

Penicillin Protection by the Calendar



not by the clock



when
you
use

Flo-Cillin "96"

Bristol Laboratories Trademark For
CRYSTALLINE PROCAINE PENICILLIN G IN OIL
(300,000 units per cc)
With Aluminum Monostearate, 2%

This remarkable development in repository penicillin therapy ends the need for *daily* injections. A single injection of 1 cc. produces therapeutic blood levels lasting 96 hours (4 days) in 90% of patients. A single injection *every other day* is considered adequate for most clinical purposes Exceptionally severe conditions may require more frequent dosage.

Bristol
LABORATORIES INC
SYRACUSE NEW YORK

Constantly Fluid · Requires No Prolonged Shaking · Will Not Clog the Needle

(In writing to advertisers, please mention the journal—it helps)

PROMPT REPAIR SERVICE

Cutting Loops Expertly Rebuilt. Reasonable. Send us your burned Loops.

BAKELITE SHEATHS REPLACED

We manufacture and Repair all types of Electro-Surgical Electrodes & Accessories. Prices upon request.

GREENWALD CO., INC.
DEPT. E GARY, INDIANA

A book that is always welcome

because its message has remained true and alive through 2500 years.

THE GENUINE WORKS OF HIPPOCRATES

- In the classical translation of Francis Adams that preserves the spirit of the original.
- Edited to give a connected picture of medicine in the Golden Age of Greece.
- Printed and bound to make a beautiful volume of four hundred pages.

Here is medical observation at its keenest. There hardly exist more accurate word pictures of sick men, more careful descriptions of their appearances. The book in its present form, free from technical annotations of former editions, stands out more than ever as a great contribution to medicine and world literature.

"This true medical bible will interest, if not fascinate all students of medicine, both general and special."—N. Y. *State Journal of Medicine.*

Edited and introduced by Emerson Crosby Kelly

390 pages 8 plates $3.00

THE WILLIAMS & WILKINS CO.
Baltimore 2, Maryland

RADON

When interstitial radiation is indicated, the ALL GOLD radon implant is recommended.

Our Radon Implants are ALL GOLD—24 Karat—and excellent for intratumoral implantation.

High temperature sterilization is possible with utmost safety.

Accurate dosage is assured because the ALL GOLD radon implant is sold with a guarantee as to radon content at hour of use.

•

Prices and Literature on Request.

RADIUM CHEMICAL COMPANY • Inc.

570 Lexington Ave., New York, 22, N. Y.
Chicago: Marshall Field Annex Building

. . . for the

Patient with

CHRONIC

Urinary Tract

Infection

The harassing urinary symptoms of frequency, pain, and burning on urination can be relieved in a high percentage of patients through the simple procedure of administering Pyridium.

In stubborn or inoperable cases, the physician can often provide the patient with almost immediate relief from these distressing symptoms during the time that other therapeutic measures are directed toward alleviating the underlying condition.

Pyridium is virtually nontoxic in therapeutic dosage and can be administered concomitantly with streptomycin, penicillin, or other specific therapy.

Following oral administration, Pyridium produces a definite analgesic effect on the urogenital mucosa. This effect of Pyridium is entirely local; it acts directly on the mucosa of the urogenital tract.

Literature on Request

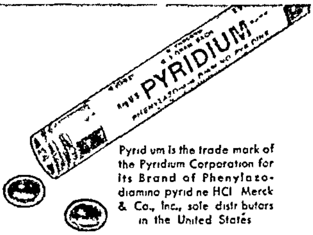
PYRIDIUM®

(Brand of Phenylazo diamino pyridine HCl)

MERCK & CO., Inc. RAHWAY, N. J.

Manufacturing Chemists

In Canada: MERCK & CO., Ltd. Montreal, Que.



Pyridium is the trade mark of the Pyridium Corporation for its Brand of Phenylazo-diamino pyridine HCl Merck & Co., Inc., sole distributors in the United States

RETROPUBIC URINARY SURGERY

by TERENCE MILLIN, F.R.C.S.
Genito-Urinary Surgeon, London

This monograph gives in detail the methods employed in the retropubic approach to a number of surgical problems. The author has had considerable success with the retropubic prostatectomy for prostatic obstructions, and also the retropubic operation for stress incontinence in women. The specially prepared illustrations are deliberately semi-diagrammatic for the sake of clarity.

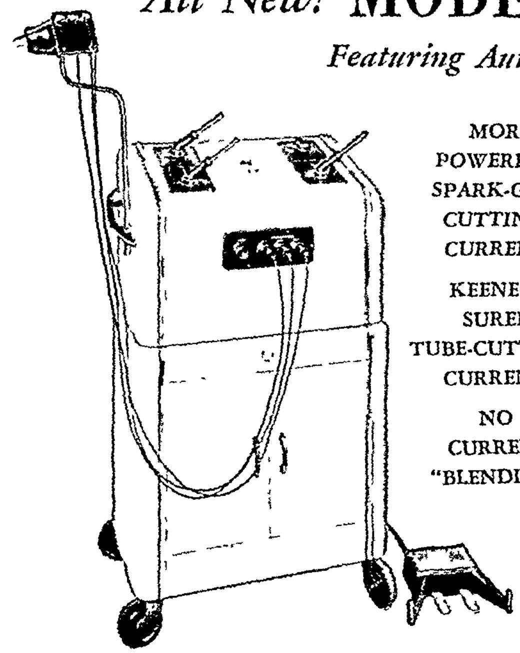
Includes Chapters on

Prostatic Obstruction
Pre- and Post-operative Care
Retropubic Prostatectomy
Fibrous and Calculous Prostate
Carcinoma of the Prostate and Bladder
Anesthesia
Appendix of Case Analyses

215 pages *163 illustrations* *$7.00*

THE WILLIAMS & WILKINS COMPANY
Mt. Royal and Guilford Aves. Baltimore 2, Md.

All New! MODEL "AG" BOVIE UNIT
Featuring Automatic Spark-Gap Adjustment



MORE POWERFUL SPARK-GAP CUTTING CURRENT

KEENER, SURER TUBE-CUTTING CURRENT

NO CURRENT "BLENDING"

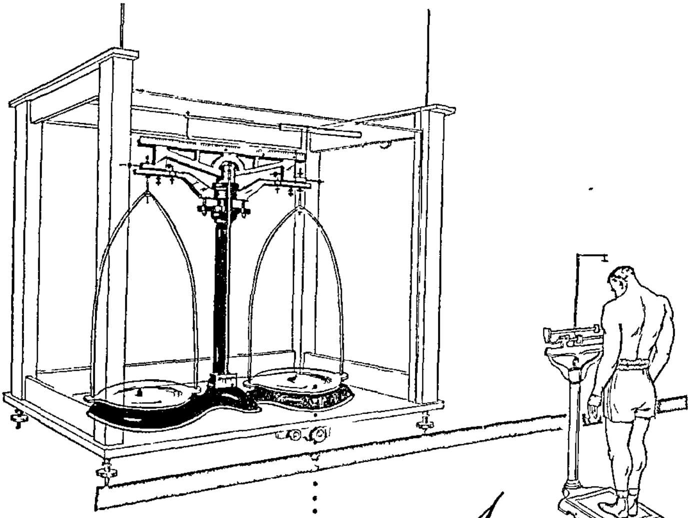
You do no current "blending" with the new "AG" Bovie—have no slow cutting, sputtering, balking current of uncertain characteristics. Five separate circuits provide you with a distinct cutting current for every cutting need: 1) Dependable, powerful spark-gap cutting current with three different degrees of hemostatic effect; 2) Spark-gap generated coagulation current; and, 3) Fast tube-cutting current, without hemostasis, the most effective tube-cutting current yet developed. In addition, wholly automatic spark-gap adjustment each time the unit is turned on insures operation at the highest level of efficiency at all times.

You Need This
Greatest Bovie of Them All

WRITE FOR DETAILS

V. Mueller and Company
408 S. HONORE STREET
CHICAGO 12, ILLINOIS

New steel cabinet and sub-cabinet have durable ivory finish, brown panels, chrome trim. Sub-cabinet has partitioned drawer for handy storage of surgical accessories. Sterilizable instrument rack adjusts to several convenient operating positions. Complete details will be sent promptly upon request.



Weighing In

for added assurance of potent penicillin

weight check for potency

One of the 138 separate tests made by Abbott in the production of dependable penicillin. This test applies only to vials and other dry powder containers. A bulk lot of penicillin powder is bio-assayed for potency, and the weight of powder required for a certain number of units is determined. In the case of pure potassium crystalline penicillin G, for instance, a filling of 126 mg. indicates a potency of 200,000 units. As the vials are filled by machine, frequent weight checks supplement the bio assays One series of checks on each lot is made [illegible] within strict weight variation limits.

The absolute dependability of Penicillin Abbott is assured by 138 separate tests made during the production process. These 138 Abbott tests—in addition to those conducted by the Food and Drug Administration—cover such important factors as potency, sterility, pyrogens, toxicity, penicillin G content, heat stability, pH, clarity, crystallinity, and moisture content. They make it possible for you to use Penicillin Abbott *with confidence* whenever penicillin therapy is required. Administration is simplified by the convenient variety of Abbott Penicillin Products—vials, cartridges, troches, tablets, *Dulcet®* tablets and ointments. All are available at prescription pharmacies everywhere. For more information about them, just write to ABBOTT LABORATORIES, North Chicago, Ill.

®Medicated Sugar Tablets, Abbott

Specify:

ABBOTT *Penicillin Products*

Second Edition

GYNECOLOGICAL AND OBSTETRICAL UROLOGY

by HOUSTON EVERETT, M.D.

Associate Professor of Gynecology, Johns Hopkins University, and Associate in Gynecology, University of Maryland; Assisting Visiting Gynecologist and Gynecologist in charge of the Cystoscopic Clinic, Johns Hopkins Hospital

Thoroughly revised and brought up to date, Doctor Everett's valuable work continues to fill a necessary place in the literature. Clear and concise, practical and comprehensive, as before, the text embodies a wide personal experience in all phases of gynecology and female urology in addition to a judicial weighing of the opinions of others working in these fields.

Additional material in the second edition includes a section on indirect cystoscopy, description and illustration of the Aldridge operation for stress incontinence, and special attention to penicillin as a therapeutic agent in urology. In addition, the section on primary neoplasms of the bladder has been almost entirely rewritten, and many of the illustrations have been replaced or improved.

The illustrations continue to play an important part in the value of the book. Not only do they support the well-written text, but they also tell their own connected story. They are keyed to the text and to each other.

"Dr. Everett has produced the most complete single volume extant on urology as applied to women . . . . . Dr. Everett has not only been able to condense the best in the literature but has given many original and practical ideas culled from his own practice."—*Southern Medical Journal*

510 pages **220 illustrations** **$6.00**

SANS TACHE

THE WILLIAMS & WILKINS COMPANY

MT. ROYAL AND GUILFORD AVES. BALTIMORE 2, MD.

Are you confused

when considering which androgenic preparation to use?

Recent conflicting statements on the relative potencies and use of various testosterone* products for parenteral administration indicate—more than ever—the wisdom of using Council-Accepted androgenic preparations.

Established therapeutic claims and approved advertising copy are assured with Testosterone Propionate "Rare", the only androgenic preparation for intramuscular use which bears the seal of acceptance of the Council on Pharmacy and Chemistry of the American Medical Association.

*Popularly known as "male sex hormone".

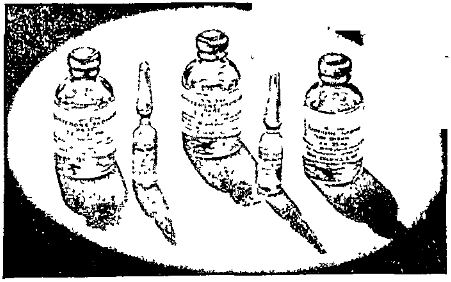
None is more potent for intramuscular use than

TESTOSTERONE PROPIONATE "Rare"

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

Testosterone Propionate "Rare":
1 cc. ampules, 5, 10 and 25 mg.
in boxes of 3, 6 and 50;
also 10 cc. vials, 25 mg. per cc.,
and 6 cc. vials, 50 mg per cc.

Methyl Testosterone "Rare":
Scored tablets, 10 mg. (white)
and 20 mg. (pink); bottles of
30 and 100.



Rare Chemicals, Inc. HARRISON, NEW JERSEY

West Coast Distributors: GALEN COMPANY, *Richmond, Calif* 1221

PLASTIC and RECONSTRUCTIVE SURGERY

The Official Periodical of the
American Society of Plastic and Reconstructive Surgery

ROBERT H. IVY, M.D., *Editor*

Here is the first and only journal devoted entirely to this growing and important specialty. As the official journal of a leading scientific organization in the field, it represents the highest ethical standards.

A broad and comprehensive editorial viewpoint makes the journal valuable to the plastic surgery and to men with plastic problems in other branches of surgery.

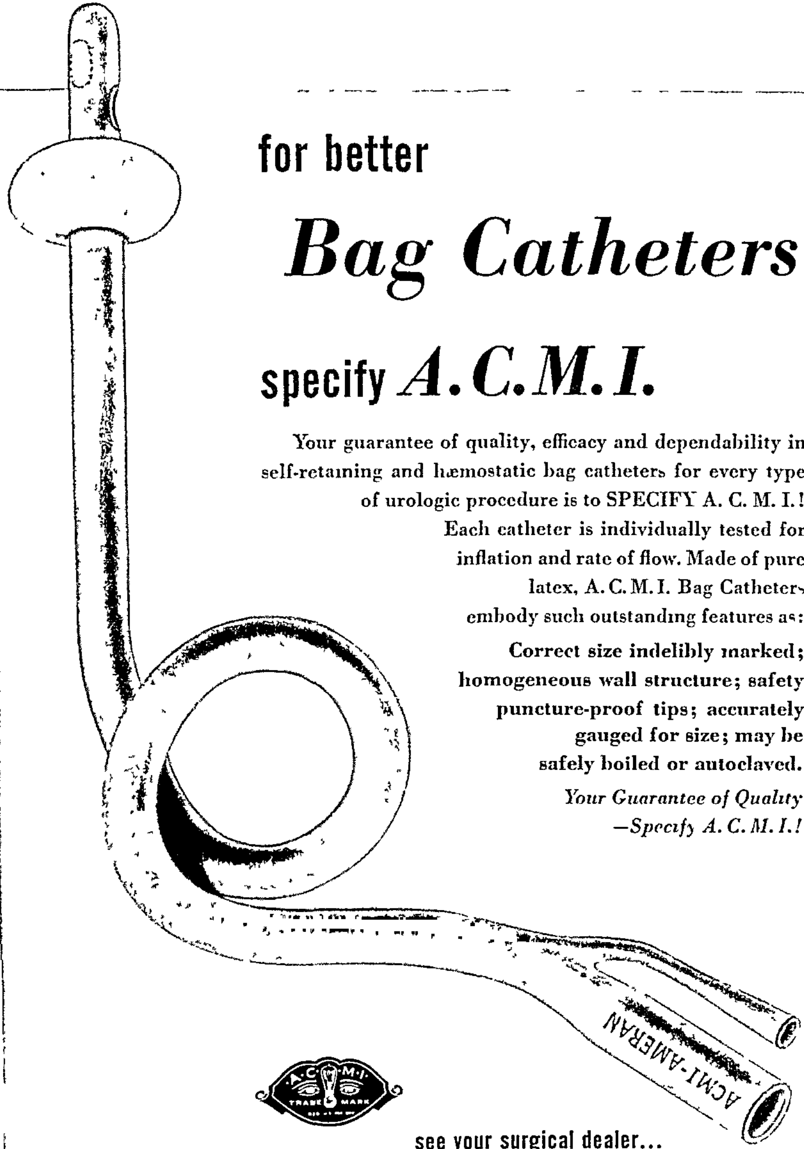
In addition to the best articles available on plastic and reconstructive surgery, the journal carries a comprehensive abstract section, and a book review section. Each issue is well illustrated, often in full color.

Published bi-monthly, one volume of about 500 pages a year, beginning January. Subscription price per volume $6.00 payable in advance.

Send your order with your remittance to the publisher

THE WILLIAMS & WILKINS COMPANY
Mt. Royal and Guilford Aves.
Baltimore 2, Md.

(In writing to advertisers, please mention the journal—it helps.)



for better

Bag Catheters!

specify *A.C.M.I.*

Your guarantee of quality, efficacy and dependability in self-retaining and hæmostatic bag catheters for every type of urologic procedure is to SPECIFY A. C. M. I.! Each catheter is individually tested for inflation and rate of flow. Made of pure latex, A. C. M. I. Bag Catheters embody such outstanding features as:

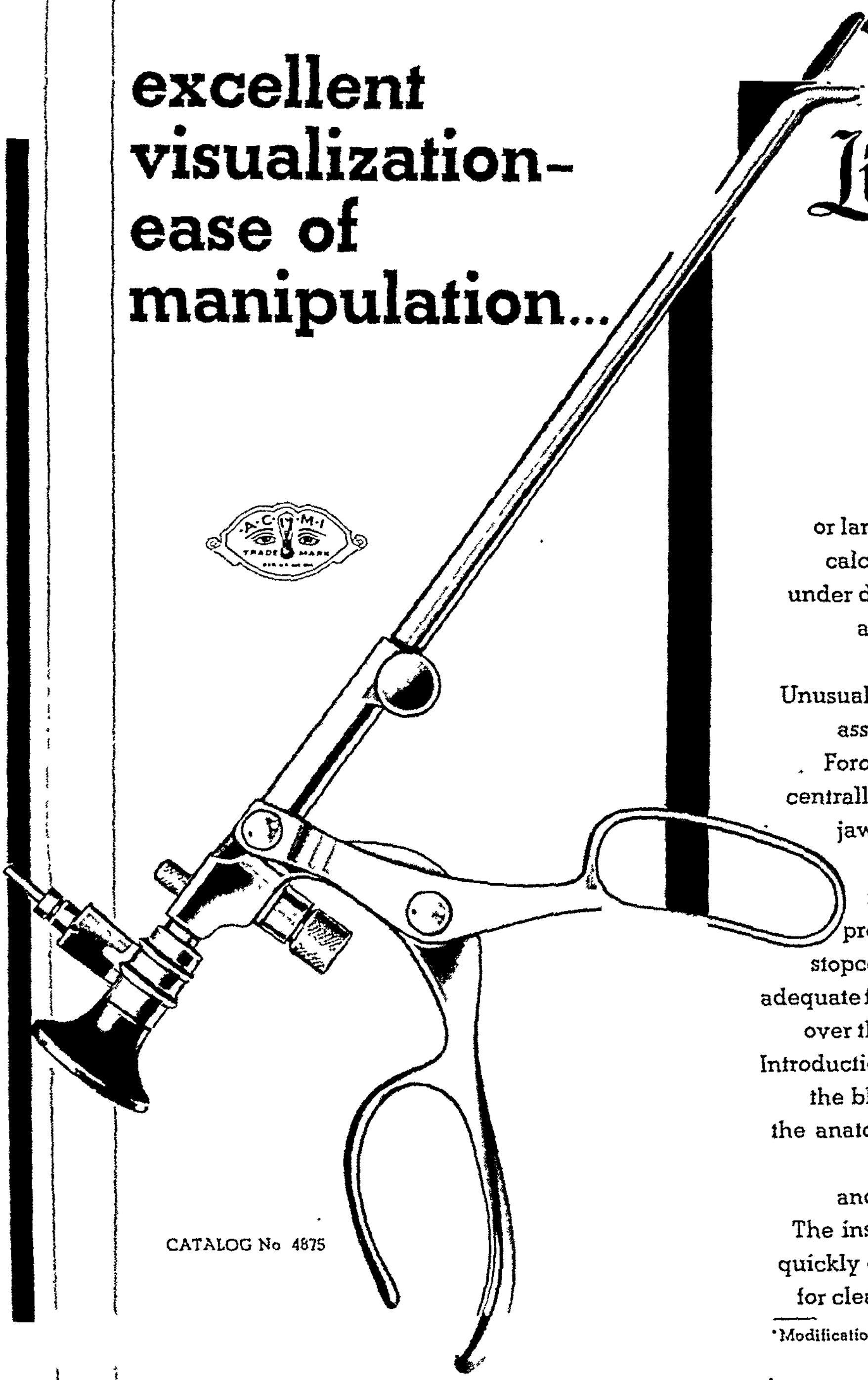
Correct size indelibly marked; homogeneous wall structure; safety puncture-proof tips; accurately gauged for size; may be safely boiled or autoclaved.

Your Guarantee of Quality
—Specify A. C. M. I.!

see your surgical dealer...

American Cystoscope Makers, Inc.
FREDERICK J WALLACE PRESIDENT

1241 LAFAYETTE AVENUE, NEW YORK 59, N. Y.



Hendrickson Lithotrite

excellent visualization– ease of manipulation...

Crushing small calculi, or large fragments of vesical calculi, may be carried out under direct vision—smoothly and certainly—with this visualizing lithotrite.* Unusually good visualization is assured by the McCarthy Foroblique 68A Telescope, centrally located between the jaws and close to the field of operation. Ample irrigation of the field is provided by large lumen stopcocks which channel an adequate flow of water, centrally, over the telescope objective. Introduction of the lithotrite into the bladder is facilitated by the anatomically correct angle of the crushing jaws and the instrument shaft. The instrument itself may be quickly disassembled after use for cleaning and sterilization.

A·C·M·I TRADE MARK

CATALOG No 4875

---

*Modification by Dr. Floyd C. Hendrickson

American Cystoscope Makers, Inc.

1241 LAFAYETTE AVENUE
FREDERICK C. WALLACE, *President*
NEW YORK 59, N. Y.

AMERICAN UROLOGICAL ASSOCIATION

OFFICERS 1948–1949

President—Dr Charles C Higgins, Cleveland Clinic, Cleveland, Ohio
President Elect—Dr Carl F Rusche, 906 Taft Building, Hollywood, California
Past President—Dr Herbert H Howard, 270 Commonwealth Avenue, Boston, Mass
Secretary—Dr Thomas D Moore, 899 Madison Ave , Memphis, Tenn
Treasurer—Dr George C Prather, 1180 Beacon Street, Brookline, Mass
Historian—Dr Wirt B Dakin, 523 W Sixth St , Los Angeles, California

EXECUTIVE COMMITTEE

New England Section—Dr Roger C Graves, 12 Bay State Rd , Boston, Mass
Alternate—Dr Fletcher H Colby, 262 Beacon St , Boston, Mass
New York Section—Dr George W Fish, 755 Park Avenue, New York, New York
Alternate—Dr Augustus Harris, 306 Park Place, Brooklyn, New York
Mid-Atlantic Section—Dr Charles H deT Shivers, 121 S Illinois Ave , Atlantic City, N J
Alternate—Dr Ralph M LeComte, 1801 Eye St , N W , Washington, D C
Southeastern Section—Dr. Hamilton W McKay, 121 W Seventh St , Charlotte, N C
Alternate—Dr J Ullman Reaves, 303 Van Antwerp Bldg , Mobile, Ala
North Central Section—Dr William J Baker, 7 West Madison Street, Chicago, Illinois
Alternate—Dr Carroll C Hyde, 122 N Lafayette Blvd , South Bend, Ind
South Central Section—Dr R Lee Hoffmann, 1019 Professional Bldg , Kansas City, Mo
Alternate—Dr H Fay H Jones, 808 Donaghey Bldg , Little Rock, Ark
Western Section—Dr Dudley P Fagerstrom, 710 Medico Dental Bldg , San Jose, Calif
Alternate—Dr A J Scholl, 1930 Wilshire Blvd , Los Angeles, Calif

Sections of the American Urological Association

NEW ENGLAND SECTION

President—Dr Edward L Peirson, 374 Essex Street, Salem, Mass
Secretary-Treasurer—Dr Richard Chute, 330 Dartmouth Street, Boston 16, Mass
Executive Committee—Chairman, Dr George C Prather, 1180 Beacon Street, Brookline 46, Mass , Dr John P Bowler Hitchcock Clinic, Hanover, N H , Dr Winthrop M Flagg, 49 South Winooski Ave , Burlington, Vt , Dr Ernest K Landsteiner, 4 George St , Providence, R I , Dr Samuel A MacDonald, 1414 Drummond St , Montreal P Q , Canada, Dr Donald F Marshall, 142 High St , Portland Maine, Dr C H Neuswanger, 89 N Main St , Waterbury, Conn , Dr Bancroft C Wheeler, 27 Elm St , Worcester, Mass

NEW YORK SECTION

President—Dr Francis P Twinem, 901 Lexington Ave , New York, N Y
Vice President—Dr Herbert M Ill, 42 Woodland Ave , Glen Ridge, N J
Secretary—Dr John N Robinson 755 Park Ave , New York, N Y
Treasurer—Dr Oscar P Schoenemann, 848 Carroll St , Brooklyn, N Y
Executive Committee—Dr John K de Vries, 144 S Harrison St , East Orange, N J , Dr George W Fish, 755 Park Ave , New York, N Y , Dr Augustus L Harris, 306 Park Place, Brooklyn, N Y , Dr Robert S Hotchkiss, 65 E 66th St , New York, N Y

NORTHEASTERN SECTION

President—Dr James C McClelland, 170 St George St , Toronto Ontario
President Elect—Dr A L Parlow, Medical Arts Bldg , Rochester, New York
Past President—Dr George E Slotkin, 333 Linwood Ave , Buffalo, New York
Secretary Treasurer—Dr Albert M Crance, 525 S Main St , Geneva, N Y
Executive Committee—Dr William A Barrett 506 Med Arts Bldg Pittsburgh Pa , Dr J Victor Berry, 180 Metcalfe St , Ottawa, Ont , Dr John L Hamilton, 7086 Jenkins Arcade, Pittsburgh, Pa , Dr William J Kennedy, 86 N Main St , Gloversville, N Y , Dr S A MacDonald, 1414 Drummond St , Montreal, Que

MID-ATLANTIC SECTION

President—Dr. Theodore R. Fetter, 255 South 17th Street, Philadelphia 3, Pa.
Vice-President—Dr. Albert E. Goldstein, 3505 N. Charles St., Baltimore 18, Md.
Secy.-Treas.—Dr. Horatio N. Dorman, 611-A Stoneleigh Court, Washington 6, D. C.
Executive Committee—Dr. Grattan G. Irwin, 801 Atlas Bldg., Charleston, W. Va.; Dr. Linwood D. Keyser, Medical Arts Bldg., Roanoke, Va.; Dr. Charles A. W. Uhle, 255 South 17th St., Philadelphia 3, Pa.; Dr. Hugh J. Jewett, 1201 N. Calvert St., Baltimore 2, Md.
Executive Committee of A.U.A.—Dr. Charles H. de T. Shivers, 121 S. Illinois Ave., Atlantic City, N. J.
Alternate—Dr. Ralph M. LeComte, 1801 Eye St., N. W., Washington, D. C.

SOUTHEASTERN SECTION

President—Dr. Harold P. McDonald, 804 Healey Bldg., Atlanta, Ga.
President-Elect—Dr. James J. Ravenel, 96 Ashley Ave., Charleston, S. C.
Past President—Dr. Robert B. McIver, 208 Laura St., Jacksonville, Florida
Secretary-Treasurer—Dr. Russell B. Carson, 314 Sweet Bldg., Ft. Lauderdale, Fla.
Executive Committee—Dr. F. Thomas Boudreau, 705 Merchant Nat'l Bank Bldg., Mobile, Ala.; Dr Willard L. Fitzgerald, 422 Ingraham Bldg., Miami, Florida; Dr. Stephen T. Brown, 205 Medical Arts Bldg., Atlanta, Georgia; Dr. W. R. Miner, 33 E. Seventh St., Covington, Kentucky; Dr. Hugh T. Beacham, 1110 Pere Marquette Bldg., New Orleans, La.; Dr. Frank L. Ramsay, Ramsay Clinic, Laurel, Mississippi; Dr. Sidney Smith, 421 Professional Bldg., Raleigh, North Carolina; Dr. William R. Barron, 1018 Calhoun St., Columbia, South Carolina; Dr. Samuel L. Raines, 188 S. Bellevue, Memphis, Tenn.
Executive Committee of A.U.A.—Dr. Hamilton McKay, *Charlotte, N. C.*
Alternate—Dr. J. Ullman Reaves, Mobile, Ala.
Editorial Committee of A.U.A.—Dr. Montague L. Boyd, Atlanta, Ga.

NORTH CENTRAL SECTION

President—Dr. James C. Sargent, 324 E. Wisconsin Ave., Milwaukee 2, Wis.
President-Elect—Dr. Russell D. Herrold, 6 North Michigan Ave., Chicago, Ill.
Secretary-Treasurer—Dr. William J. Engel, 2020 E. 93rd Street, Cleveland 6, Ohio
Executive Committee—Dr. Carroll C. Hyde, 122 N. Lafayette Blvd., South Bend, Ind.; Dr. John L. Emmett, Mayo Clinic, Rochester, Minnesota; Dr. Reed M. Nesbit, University Hospital, Ann Arbor, Mich.; Dr. John B. Wear, 1 S. Pinckney St., Madison 3, Wisconsin; Dr. Leo P. Dolan, 1052 Edison Bldg., 420 Madison Ave., Toledo, Ohio; Dr. Edward M. Honke, 618 Davidson Bldg., Sioux City 13, Iowa; Dr. Robert S. Breakey (*ex-officio*), 1211 Bank of Lansing Bldg., Lansing 16, Michigan; Dr. William J. Baker (*ex-officio*), 7 West Madison St., Chicago 2, Illinois.

SOUTH CENTRAL SECTION

President—Dr. W. Joseph McMartin, 611 City National Bank Bldg., Omaha, Nebr.
Vice-President—Dr. E. Halsell Fite, 7th Fl. Commerce National Bank, Muskogee, Okla.
Secretary-Treasurer—Dr. Harry M. Spence, 4105 Live Oak St., Dallas 1, Texas
Executive Committee—Dr. Neil S. Moore, 729 Frisco Bldg., St. Louis, Missouri; Dr. E. E. Angle, 903 Sharp Bldg., Lincoln, Nebraska; Dr. R. H. Akin, 610 N.W. Ninth St., Oklahoma City, Okla.; Dr. John F. Patton, 723 University Club Bldg., St. Louis, Mo.; Dr. D. R. Higbee, 1117 Republic Bldg., Denver Colorado; Dr. H. E. Neptune, 617 United Life Bldg., Salina, Kansas; Dr. C. M. Crigler, 1006 Esperson Bldg., Houston, Texas; Dr. H. King Wade, Wade Bldg., Hot Springs, Arkansas; Dr. V. E. Berchtold, 206 Coronado Bldg., Santa Fe, N. Mexico; Dr. Santiago Blanco, Calle 60 num. 543, Merida, Yucatan, Mex.

WESTERN SECTION

President—Dr. Carl F. Rusche, 1680 N. Vine St., Hollywood, Calif.
President-Elect—Dr. Arno G. Folte, 870 Market St., San Francisco, Calif.
Past President—Dr. John R. Hand, 1216 S. W. Yamhill St., Portland, Oregon
Secretary-Treasurer—Dr. Adolph A. Kutzmann, 1930 Wilshire Blvd., Los Angeles, Calif.
Executive Committee—Dr. Frederick A. Bennetts, 1921 Wilshire Blvd., Los Angeles, Calif.; Dr. Frank J. Clancy, 1305 Fourth Ave., Seattle, Wash.; Dr. Charles D. Donahue, 631 Miner Bldg., Eugene, Oregon; Dr. Ivan L. Finkelberg, 208 Central Bldg., San Bernardino, Calif.; Dr. George M. Fister, 385 24th St., Ogden, Utah; Dr. Lloyd E. Kindall, 400 29th St., Oakland, California.

(*Branch Societies listed on Cover 3*)

REGISTRY OF GENITO-URINARY PATHOLOGY

The following members of the Registry of Genito Urinary Pathology are eager to assist you in registering tumors of the genito urinary organs, in obtaining the advantages of the consultation service or in obtaining information regarding the Registry publications or loan sets of microscope slides Please communicate with the Committee member nearest you regarding the registration of tumors Communications regarding the other functions of the Registry can be made directly to Col J E Ash, Army Institute of Pathology, Washington, D C

CALIFORNIA

Tracy O Powell, 915 Equitable Bldg , 6253 Hollywood Blvd , Los Angeles 28
Thomas E Gibson, 450 Sutter St , San Francisco

DISTRICT OF COLUMBIA

Col J E Ash, Army Institute of Pathology, Washington
William P Herbst, 1801 Eye St , N W , Suite 314, Washington 6

FLORIDA

Louis M Orr, 307 S Orange Ave , Orlando

GEORGIA

Harold P McDonald, The Ballenger McDonald Clinic, 804–810 Healey Bldg , 57 Forsyth St , Northwest, Atlanta 3

ILLINOIS

William J Baker, 7 W Madison St , Chicago 2

INDIANA

William Niles Wishard, Jr , 1711 N Capitol Ave , Indianapolis

IOWA

Rubin Flocks, University Hospitals Iowa City

LOUISIANA

Edgar Burns, Ochsner Clinic, Prytania and Aline Sts , New Orleans 15

MARYLAND

W Houston Toulson, Medical Arts Bldg , Baltimore 1

MASSACHUSETTS

Richard Chute, 330 Dartmouth St , Boston
Roger C Graves, 12 Bay State Road, Boston
George C Prather, 1180 Beacon St , Brookline 46

MICHIGAN

Reed M Nesbit, University Hospital, Ann Arbor

MINNESOTA

Gershom, J Thompson, Mayo Clinic, Rochester

MISSOURI

Nelse F Ockerblad, 1530 Professional Bldg , Kansas City
E Humber Burford, 958 Arcade Bldg St Louis
Otto J Wilhelmi, 218–220 University Club Bldg , St Louis 3

NEBRASKA

William Joseph McMartin, 611 City National Bank Bldg , Omaha 2

NEW JERSEY

W Kenneth Wheeler, 140 Roseville Ave , Newark 7

MID-ATLANTIC SECTION

President—Dr. Theodore R. Fetter, 255 South 17th Street, Philadelphia 3, Pa.
Vice-President—Dr. Albert E. Goldstein, 3505 N. Charles St., Baltimore 18, Md.
Secy.-Treas.—Dr. Horatio N. Dorman, 611-A Stoneleigh Court, Washington 6, D. C.
Executive Committee—Dr. Grattan G. Irwin, 801 Atlas Bldg., Charleston, W. Va.; Dr. Linwood D. Keyser, Medical Arts Bldg., Roanoke, Va.; Dr. Charles A. W. Uhle, 255 South 17th St., Philadelphia 3, Pa.; Dr. Hugh J. Jewett, 1201 N. Calvert St., Baltimore 2, Md.
Executive Committee of A.U.A.—Dr. Charles H. de T. Shivers, 121 S. Illinois Ave , Atlantic City, N. J.
Alternate—Dr. Ralph M. LeComte, 1801 Eye St., N. W., Washington, D. C.

SOUTHEASTERN SECTION

President—Dr. Harold P. McDonald, 804 Healey Bldg., Atlanta, Ga.
President-Elect—Dr. James J. Ravenel, 96 Ashley Ave., Charleston, S. C.
Past President—Dr. Robert B. McIver, 208 Laura St., Jacksonville, Florida
Secretary-Treasurer—Dr. Russell B. Carson, 314 Sweet Bldg., Ft. Lauderdale, Fla.
Executive Committee—Dr. F. Thomas Boudreau, 705 Merchant Nat'l Bank Bldg., Mobile, Ala.; Dr Willard L. Fitzgerald, 422 Ingraham Bldg., Miami, Florida; Dr. Stephen T. Brown, 205 Medical Arts Bldg., Atlanta, Georgia; Dr. W. R. Miner, 33 E. Seventh St., Covington, Kentucky; Dr. Hugh T. Beacham, 1110 Pere Marquette Bldg., New Orleans, La.; Dr. Frank L. Ramsay, Ramsay Clinic, Laurel, Mississippi; Dr. Sidney Smith, 421 Professional Bldg., Raleigh, North Carolina; Dr. William R. Barron, 1018 Calhoun St., Columbia, South Carolina; Dr. Samuel L. Raines, 188 S. Bellevue, Memphis, Tenn.
Executive Committee of A.U.A.—Dr. Hamilton McKay, Charlotte, N. C.
Alternate—Dr. J. Ullman Reaves, Mobile, Ala.
Editorial Committee of A.U.A.—Dr. Montague L. Boyd, Atlanta, Ga.

NORTH CENTRAL SECTION

President—Dr. James C. Sargent, 324 E. Wisconsin Ave., Milwaukee 2, Wis.
President-Elect—Dr. Russell D. Herrold, 6 North Michigan Ave., Chicago, Ill.
Secretary-Treasurer—Dr. William J. Engel, 2020 E. 93rd Street, Cleveland 6, Ohio
Executive Committee—Dr. Carroll C. Hyde, 122 N. Lafayette Blvd., South Bend, Ind.; Dr. John L. Emmett, Mayo Clinic, Rochester, Minnesota; Dr Reed M. Nesbit, University Hospital, Ann Arbor, Mich.; Dr. John B. Wear, 1 S. Pinckney St., Madison 3, Wisconsin; Dr. Leo P. Dolan, 1052 Edison Bldg., 420 Madison Ave., Toledo, Ohio; Dr. Edward M. Honke, 618 Davidson Bldg., Sioux City 13, Iowa; Dr. Robert S. Breakey (*ex-officio*), 1211 Bank of Lansing Bldg., Lansing 16, Michigan; Dr. William J. Baker (*ex-officio*), 7 West Madison St., Chicago 2, Illinois.

SOUTH CENTRAL SECTION

President—Dr. W. Joseph McMartin, 611 City National Bank Bldg., Omaha, Nebr.
Vice-President—Dr. E. Halsell Fite, 7th Fl. Commerce National Bank, Muskogee, Okla.
Secretary-Treasurer—Dr. Harry M. Spence, 4105 Live Oak St., Dallas 1, Texas
Executive Committee—Dr. Neil S. Moore, 729 Frisco Bldg., St. Louis, Missouri; Dr. E. E. Angle, 903 Sharp Bldg., Lincoln, Nebraska; Dr. R. H. Akin, 610 N.W. Ninth St., Oklahoma City, Okla.; Dr. John F. Patton, 723 University Club Bldg., St. Louis, Mo.; Dr. D. R. Higbee, 1117 Republic Bldg., Denver Colorado; Dr. H. E. Neptune, 617 United Life Bldg., Salina, Kansas; Dr. C. M. Crigler, 1006 Esperson Bldg., Houston, Texas; Dr. H. King Wade, Wade Bldg., Hot Springs, Arkansas; Dr. V. E. Berchtold, 206 Coronado Bldg., Santa Fe, N. Mexico; Dr. Santiago Blanco, Calle 60 num. 543, Merida, Yucatan, Mex.

WESTERN SECTION

President—Dr. Carl F. Rusche, 1680 N. Vine St., Hollywood, Calif.
President-Elect—Dr. Arno G. Folte, 870 Market St., San Francisco, Calif.
Past President—Dr. John R. Hand, 1216 S. W. Yamhill St., Portland, Oregon
Secretary-Treasurer—Dr. Adolph A. Kutzmann, 1930 Wilshire Blvd., Los Angeles, Calif.
Executive Committee—Dr. Frederick A. Bennetts, 1921 Wilshire Blvd., Los Angeles, Calif.; Dr. Frank J. Clancy, 1305 Fourth Ave., Seattle, Wash.; Dr. Charles D. Donahue, 631 Miner Bldg., Eugene, Oregon; Dr Ivan L. Finkelberg, 208 Central Bldg., San Bernardino, Calif.; Dr. George M. Fister, 385 24th St., Ogden, Utah; Dr. Lloyd E. Kindall, 400 29th St., Oakland, California.

(Branch Societies listed on Cover 3)

Vol. 61, No 1, Jan, 194

RAYOPAKE 'ROCHE'

- new contrast medium

WATER-SOLUBLE

RAPIDLY ABSORBABLE

HIGHLY VISCOUS

Rayopake greatly facilitates X-ray studies of the uterus, fallopian tubes, bladder, and urethra because it offers clinically valuable advantages. Since Rayopake *is water-soluble, it is rapidly absorbed and there is no danger of foreign body* reactions, retention cysts, or other complications due to the use of oily substances. While Rayopake is distinguished by clinically desirable viscosity, it does not *have a tendency to foam, thereby obviating the likelihood of false X-ray shadows.* Over twenty published reports have confirmed the clinical usefulness of this new contrast medium. Rayopake is available in vials of 7½ cc (for uterosalpingography) and 35 cc (for cystourethrography). *For samples and* descriptive literature write to Department R-4.

T.M. — Rayopake — Reg U S Pat Off Rayopake is a viscous, aqueous solution containing 50 percent diethanolamine salt of 2,4 dioxo 3 iodo 6 methyl tetrahydropyridine N-acetic acid and 4 8 percent polyvinyl alcohol

HOFFMANN-LA ROCHE INC • ROCHE PARK • NUTLEY 10 • N. J.

Continued from Front Cover

Hypospadias. *A. I. Dodson* 116
Streptomycin in Urogenital Tuberculosis. *L. Herman* 122
Bacillus Lactis Aerogenes in Urinary Tract Infections. *S. F. Wilhelm and L. A. Orkin* 131
Discussion 140
Pseudohermaphroditism. *C. L. Deming, J. B. Goetsch and F. D. Humm* 144
A Percussion Lithotrite. *H. E. Carlson* 155
Discussion 157

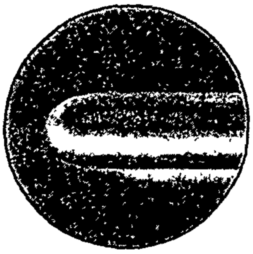
The New York Section will meet November 17, 1948, February 16, 1949, and on April 20, 1949

Annual Meeting, Western Section, Coronado Hotel, Coronado, Calif., January 17, 18, 19, 1949

Annual Meeting, Southeastern Section, Boca Raton Club, Boca Raton, Florida, March 21, 22, 23, 24, 1949

Annual Meeting, Mid-Atlantic Section, Claridge Hotel, Atlantic City, N. J., March 31, April 1 and 2, 1949

Annual Meeting, South Central Section, Broadmoor Hotel, Colorado Springs, Colo., October 17, 18, 19, 1949



RADON SEEDS

FOR safety and reliability use composite Radon seeds in your cases requiring interstitial radiation. The Composite Radon Seed is the only type of metal Radon Seed having smooth, round, non-cutting ends. In this type of seed, illustrated here highly magnified, Radon is under gas-tight, leak-proof seal. Composite Platinum (or Gold) Radon Seeds and loading-slot instruments for their implantation are available to you exclusively through us. Inquire and order by mail, or preferably by telegraph, reversing charges.

THE RADIUM EMANATION CORPORATION
GRAYBAR BLDG. Telephone MU 3-8636 NEW YORK, N. Y.

(In writing to advertisers, please mention the journal—it helps.)

THE JOURNAL OF UROLOGY
Vol 61, No 1, January 1949
Printed in U.S A

TWO UNUSUAL CAUSES OF RENAL HEMATURIA[1]

HAMILTON W McKAY, H HAYNES BAIRD AND KENNETH M LYNCH, JR

During the past year we have of necessity performed nephrectomies on 2 patients who presented severe intractible unilateral hematuria due to causes which we were unable to ascertain prior to postoperative examination of the kidney The kidney in 1 case showed a vascular lesion of a papilla which we prefer to call a hamartoma, and the other an inflammatory process with ulceration of a papilla These cases have stimulated us to review the literature on so-called essential hematuria in general and on vascular irregularities and non-specific infectional processes of the renal papilla in particular It is our purpose in this paper to present our 2 cases in some detail, to review the literature compiling previously reported cases, and to present the conclusions reached through our experience and investigation

We should like to state that we prefer such a term as unexplained hematuria to the commonly used term essential hematuria We believe, as does Kretschmer, that all kidneys which bleed will show lesions of some kind if adequately examined[2] We feel that the term essential hematuria, like idiopathic hematuria, connotes the presence of some sort of obscure process which is physiological Randall, for example, has postulated chronic passive congestion as a cause of hematuria[3]

CASE REPORTS

Case 1 (G S H No 29725) W G , a 39 year old colored laborer, first noticed blood in his urine 3 years prior to admission to the hospital on February 18, 1947 This episode of bleeding lasted only several days and he did not consult a physician Three months prior to admission he again noticed blood in his urine and consulted us because the bleeding continued The bleeding was not associated with pain or any symptoms of urinary tract irritation On cystoscopy the urethra and bladder were found to be entirely normal in appearance Blood was seen to come from the left ureteral orifice The left pyelogram showed no abnormality The bleeding time, clotting time, and platelet count were normal, and a clinical pathologist (Dr T H Byrnes) found no evidence of blood dycrasia in a blood smear Between this examination and his admission to the hospital the left kidney pelvis was catheterized on 3 occasions and irrigated with 1 per cent silver nitrate solution each time without any demonstrable effect on the bleeding, which continued During this 3 month period the patient thought that he lost from 10 to 15 pounds in weight and prior to admission began to feel weakened and was forced to stop working

Physical examination on admission to the hospital revealed a well developed and well nourished colored man in no distress The physical examination revealed no abnormalities. Laboratory studies showed a red blood count of 4,200,000, hemoglobin 80 per cent of normal, white blood count 6,000 with normal differential count, and a negative blood Kahn. The urine was grossly bloody, the pH 5, the specific gravity 1.015, sugar negative, albumin 2 plus, the microscopic examination negative except for blood. A urine culture was negative. Excretory urography showed good function from both kidneys with no abnormalities of the pyelograms or ureterograms. A left retrograde pyelogram was no different from that made 3 months previously. A nephrectomy was performed. Several small aberrant vessels were encountered at the upper pole of the kidney; otherwise the anatomy was unremarkable. No evidence of acute or chronic inflammation was encountered in the perinephric tissues. There were no constricting elements about the kidney pedicle or ureter. When removed the kidney was entirely normal in appearance. The report of the pathologist (Dr. T. H. Byrnes) was as follows: "The specimen consists of a kidney of normal shape, 4.5 by 6 by 12 cm. The cortex is smooth except for a few retention cysts. The substance is soft, of normal color, and shows a normal ratio of medulla to cortex. The ureter, pelvis, and calyces are not dilated. The tip of one pyramid in the midportion of the kidney is slightly red. In this pyramid there is a collection of dilated veins with hemorrhage into the surrounding tissue (figures 1 and 2). The veins are markedly increased in size but no increase in the number of veins is noted. One microscopic section demonstrates a rupture of a dilated vein into the pelvis of the kidney. There is no evidence of inflammatory cells or any increase in connective tissue either about the dilated veins or in any other part of the kidney. The arteries are normal in appearance. There is no evidence of compression of the surrounding tissues by the veins."

---

[1] Read at annual meeting, Southeastern Section, American Urological Association, Hollywood, Fla , January 9, 1948

[2] J A M A , 63 2112, 1914

[3] J A M A , 60 10, 1913

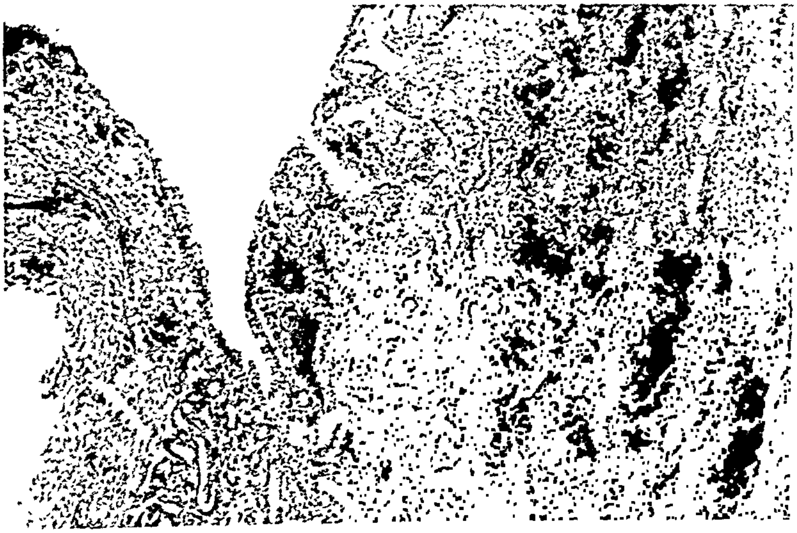


FIG. 1. Photomicrograph of section through papilla showing large veins.

Case 2. (C.M.H. No. 62906.) M. S., a 67 year old white housewife, first noticed gross hematuria 4 days prior to admission to the hospital on April 15, 1947. She had no symptoms other than mild burning on urination which she noticed several hours prior to discovering the hematuria. She had had no chills. A review of her past history revealed no symptoms of past urinary tract disease despite 4 pregnancies. She gave no history of epistaxis or other evidence of blood dyscrasia. There was no family history of tuberculosis. Physical examination revealed a moderately active woman for her age in no discomfort. The physical examination revealed no abnormalities other than slight tenderness on palpation of the right upper and lower quadrants. There was no rigidity and no palpable mass. The blood pressure was 130 mm. of mercury systolic and 70 diastolic. The temperature was 98.6 F., pulse 78, respirations 20 per minute. A catheterized bladder urine specimen was grossly bloody with a specific gravity of 1.016, pH of 5.0, a 1 plus albumin determination and a negative sugar determination. A urine culture was negative and three consecutive 24 hour urine specimens showed no acid fast bacilli. The white blood count was 12,000 with 75 per cent neutrophiles and 25 per cent lymphocytes. The red blood count was 4.0 million and the hemoglobin 11.8 grams or 81 per cent. The blood Kahn test was negative and the blood nonprotein nitrogen was 35 mg. per cent. The platelet count was 480,000, bleeding time 1 minute and 6 seconds, coagulation time 3 minutes and 39 seconds, the prothrombin time 90 per cent of normal. On cystoscopy the bladder was found filled with blood clots. The mucosa was normal in appearance except for some edema and reddening of the right ureteral orifice from which blood was seen to come. A catheter was passed to the right kidney meeting no obstruction, but no urine was obtained. A retrograde pyelogram showed a dilated pelvis with numerous rounded filling defects in the calyces,

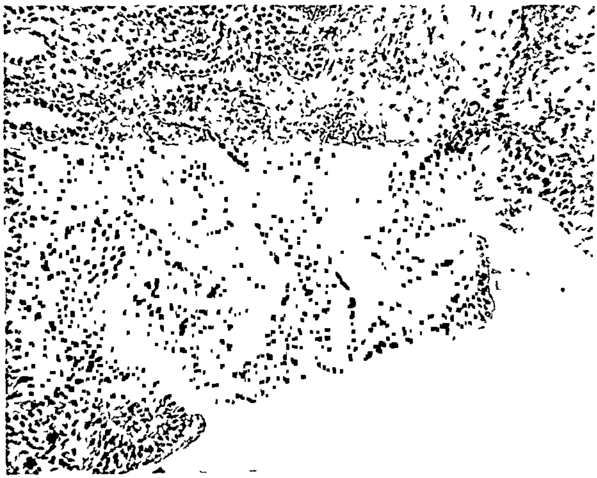


FIG. 2 Photomicrograph of section through papilla showing large veins beneath pelvic mucosa.

pelvis, and upper ureter (fig. 3, *A*). The upper ureter was somewhat larger than usual. Intravenous urography showed absence of function on the right side and good function on the left side, although the pyelogram was bizarre in appearance (fig. 3, *A*). This latter was thought to be an anomaly of the kidney. X-rays of chest and bones showed no evidence of metastasis. The patient continued to pass grossly bloody urine and for this reason was transfused with 500 cc whole blood on the third hospital day. She began to run a low grade fever with peaks at 100 F. On the sixth hospital day her hemoglobin had fallen to 73 per cent and she was again transfused with 500 cc whole blood. On the seventh hospital day cystoscopy was repeated and approximately 150 cc of blood clots were evacuated from the bladder. Clear urine was seen coming from the left ureteral orifice and blood from the right. Catheters were passed to both kidneys. Gross blood was obtained from the right; the specimen from the left kidney was clear yellow and contained no white cells, red cells, or albumin. A repeat right retrograde pyelogram showed a markedly dilated ureter and a dilated pelvis shadow (fig. 3, *B*). No dye penetrated into the pelvis. She was transfused for the third time on the eighth hospital day following which the hemoglobin level was 84 per cent. On the ninth hospital day a right nephrectomy was performed through a lumbar incision. Adequacy of the left kidney was assumed on the basis of an unelevated nonprotein nitrogen blood level, good function on excretory urography, normal urine, and despite the unusual pyelogram which suggested congenital nonrotation of the kidney (fig. 3, *B*). The case was presented at a urological staff meeting and it was the unanimous opinion that nephrectomy should be performed.

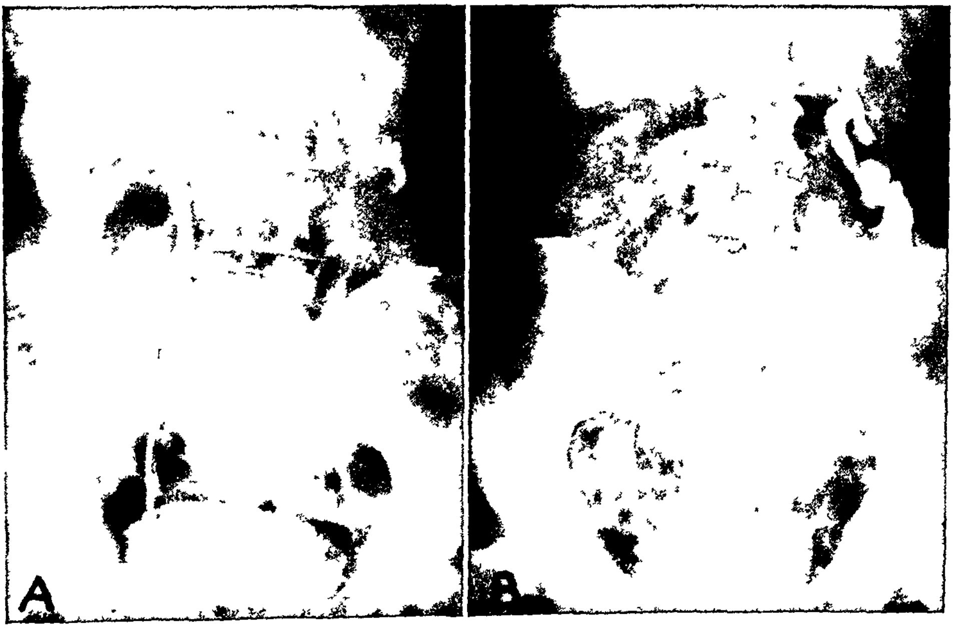


FIG. 3 *A*, Excretory left pyelogram and retrograde right pyelogram *B*, Bilateral retrograde pyelogram

On exposure of the kidney the pelvis was found to be markedly dilated and tense as was the ureter as far as it could be palpated. The ureter was a bluish color and was fully as large as the index finger. It was ligated and severed just superior to the point where it crossed the iliac artery. The patient received a fourth transfusion of 500 cc whole blood on the operating table and stood the procedure nicely, her blood pressure rising from 110 mm. of mercury to 140 mm. of mercury during the operation.

The pathological report (Dr. Paul Kimmelstiel) was as follows: "The kidney measures 12 by 6 by 4.5 cm. and weighs 145 gm. The capsule strips with ease in some portions, elsewhere it strips with some difficulty, leaving a rather smooth, occasionally granular surface. It varies in color from pinkish-gray to mottled red at which point are encountered numerous punctate partially confluent foci of hemorrhage. The kidney is sectioned revealing that the calices and pelvis are moderately dilated and distended with blood clot. The pyramids are flattened at the apices (fig. 4, *A*). At the lower pole is encountered a pyramid, the apex of which contains numerous small foci of hemorrhage and from which a small amount of sanguineous fluid can be expressed. The mucosa of the calyx adjacent to this is somewhat hemorrhagic and appears to be ulcerated at this point (fig. 4, *B*). Elsewhere in one of the upper poles a pyramid adjacent to its apex is also partially altered by a focus of deep red hemorrhage. All of the pyramids which are recognizable contain Randall's nodes. Dilatation extends into the ureter. At the ureteropelvic junction the mucosa is somewhat altered by the presence of a small number of punctate, partially confluent foci of hemorrhage. Histologic sections through various portions of the kidney (fig. 5), particularly those including the grossly hemorrhagic papillae, show an extensive inflammatory infiltration in the medullary and peripelvic portion consisting of lymphocytes, eosinophils, and in some places numerous polymorphonuclear leukocytes. Also there is found granulation tissue which is moderately rich in capillaries. Other foci of inflammatory infiltration with small round cells are found at the cortico-medullary junction and even in the cortex, connected with occasional foci of scarring in the cortex. The inflammatory infiltration is found to be rather extensive around the peripelvic veins and in one area the histologic findings are suggestive of a direct continuity between a moderate-sized vein and a markedly inflamed portion of the calyx. In this area is also found extensive necrosis of the peripelvic tissue with massive hemorrhage. In the immediate vicinity of one of those areas are found occasional multinucleated giant cells, apparently buddings of incompletely developed capillaries. Interpretation: Focal, partially necrotizing pyelonephritis in isolated calyces with massive hemorrhage."

REVIEW OF LITERATURE

A review of the literature has discovered 18 cases diagnosed as renal varix and 54 cases diagnosed as angioma of the kidney.

In 1904 Fenwick reported 6 cases of a somewhat similar nature with unilateral hematuria in which the lesions appeared to be changes in the blood supply about the renal papillae.[4] In 1 case, an 18 year old white woman on whom a papil-

---

[4] Clinical Cystoscopy. London: 1904.

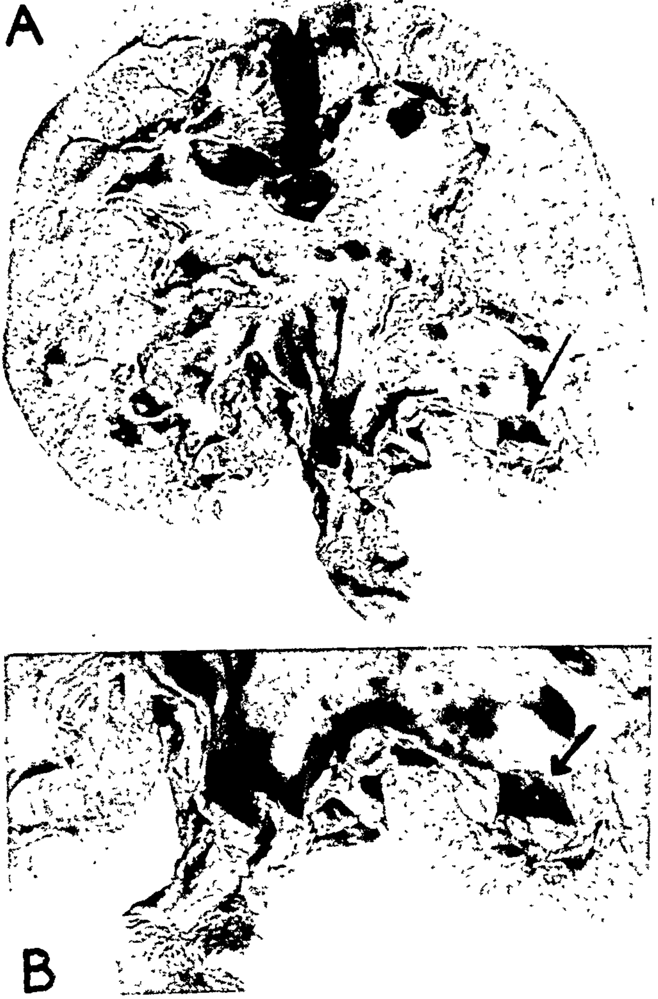


FIG. 4. *A* and *B*, Arrow points to ulcer in mucosa

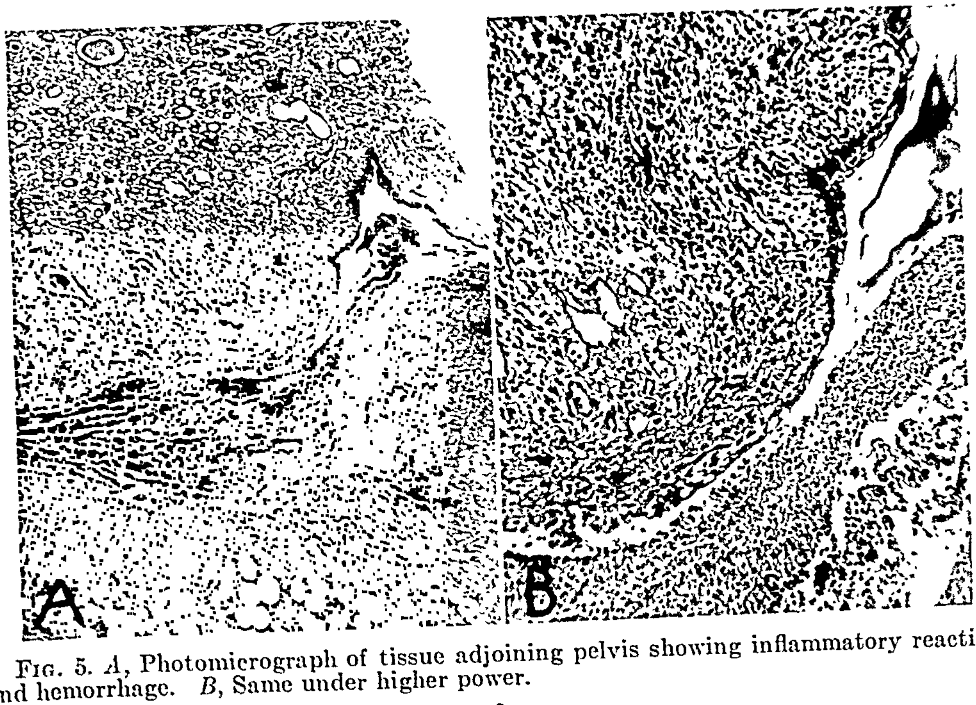


FIG. 5. *A*, Photomicrograph of tissue adjoining pelvis showing inflammatory reaction and hemorrhage. *B*, Same under higher power.

lectomy was performed because of intermittent hematuria of 5 years duration, "the vessels of the mucous membrane covering the papilla were markedly varicose. There was no evidence of growth, but there was congestion of the vessels with extravasation of blood and an increase in the cellular stroma." In another case, a woman on whom a papillectomy was performed because of hemorrhage from the left side of 2 weeks' duration, the papilla was described as being in a "bright red varicosed condition with the vessels distended with blood and some extravasation." A third case, a 40 year old white woman with unilateral hematuria from the right side of 2 years' duration, was first subjected to blind nephrotomy and subsequently to nephrectomy since the bleeding persisted. Examination of the kidney showed "dark purple papillae with extensive dilatation of small vessels constituting a capillary nevus or angioma." The lesions in the remaining 3 cases were not visualized and are therefore not included in our statistics.

Fenwick used the term varicose or varicosed in describing 2 of his cases and referred to the third as an angioma. Authors reporting subsequent similar cases have specificially used one term or the other. Those adherring to the belief that these lesions are varicosities have subsequently reported 16 additional cases. Cabot[5] and Pilcher[6] reported one each in 1909, Payne and MacNider 3 in 1916,[7] Stevens one in 1922,[8] MacGowan 3 in 1923,[9] Priestley and Wilbur 4 in 1934,[10] Bobbitt, Hoffman, and Werthammer[11] 2 in 1944, and Sporer and Pollock 1 in 1947.[12] In all of these cases there was no abnormality of the pyelograms. In all nephrectomy was performed because of severe, uncontrollable hematuria. In all except the case of Sporer and Pollock the lesion was of minute size.

A compilation of all reported cases of angioma of the kidney was published by Riley and Swann in 1941[13] and an additional case reported. They included the case which Fenwick had described as an angioma and 36 others. The lesion in most of these cases was large enough to cause a filling defect on pyelography. A few were minute and caused no abnormality of the pyelogram. These latter were pathologically similar to the cases reported as varices of the renal papilla. Of the 37 cases nephrectomy had been performed in 33, papillectomy in one, and 3 had been discovered at autopsy. In 3 cases nephrectomy had been preceded by nephrotomy and/or decapsulation. Dorman and Fowler in 1946[14] bring the total of cases diagnosed as angioma of the kidney to 54. They include the 3 cases of MacGowan which they state are definitely cases of angioma and not renal varix. We have deleted 2 of these cases in our chart as Fenwick reports them as cases of varix. White and Braunstein reported an additional case in 1946[15] and Lownes, Baron, and Lipshutz a case in 1947.[16]

---

[5] Am. J. Med. Sci., 137: 98, 1909.
[6] Ann. Surg., 49: 652, 1909.
[7] J. A. M. A., 67: 918, 1916.
[8] J. A. M. A., 79: 1302, 1922.
[9] J. Urol., 9: 331, 1923.
[10] Proc. Staff Meet., Mayo Clinic, 9: 348, 1934.
[11] J. Urol., 52: 288, 1944.
[12] J. Urol., 58: 424, 1947.
[13] Urol. & Cutan. Rev., 45: 377, 1941.
[14] J. Urol., 55: 348, 1946.

The paucity in the literature of cases resembling our second case is surprising. They are more often referred to in the discussion of papers on essential hematuria than they are formally reported. In 1914 Braasch,[17] in discussing a paper by Spitzer[18] on "continuous painless renal hemorrhage", mentions "several" cases of his own in which nephrectomy was performed for intractible bleeding and the kidneys found to show what he called chronic papillitis. He stated that the urine contained a varying number of pus cells and often colon bacilli. In 1920 Quinby[19] reported 2 cases similar to our second case. The pyelograms were normal in both cases. In his first case "the pelvis was studded with red, punctate areas, especially abundant, about the orifices of the calyces" and there was no evidence of inflammatory reaction. Goodpasture examined the kidney and stated that "vascular distention, rupture, and hemorrhage" were the essential features and could have been caused by "injury to the thin vascular walls by some circulating injurious agent." In Quinby's second case the "pelvic mucosa was dark red with grayish white exudate." Microscopic examination showed "distinct inflammatory reaction and evidence of vascular injury." Goodpasture felt that there was "distinct evidence of vascular injury which might be possibly explained on the assumption of the presence of bacteria or of a local injurious agent within the lesions." There were no pus cells in the urine in either of these cases and the pre-operative urine cultures and cultures of the gross specimens were negative in both cases. Cabot in a discussion of Steven's[8] paper in 1922 correlates Quinby's second case with 7 cases of his own with chronic infection of the renal pelvis and gross hematuria. He does not mention whether pyuria and a positive urine culture were present in his cases. In 1924 MacGowan reported a case with a negative urine culture in which the pathological diagnosis was chronic hemorrhagic papillitis.[9] In 1942 Cahill reported that in 14,000 urological hospital admissions over a 10 year period there were 29 cases in which there was hematuria of unexplained origin.[20] Three nephrectomies were performed in this group and 2 of the kidneys were found to show "chronic inflammatory and vascular changes in the papillae." The cases were not further described. These few cases, 3 accurately studied and reported, and some 12 merely mentioned, represent so far as we have been able to ascertain all that have contributed to the literature on this subject.

DISCUSSION

Our 2 cases, together with those reviewed, fall readily into two groups, one including the cases of vascular irregularities whether they be classified as renal varix or angioma, and the other including the cases which show lesions interpreted by the pathologist as inflammatory in nature.

---

[15] J. Urol., 56: 183, 1946.
[16] J. Urol., 58: 417, 1947.
[17] In discussion, J. A. M. A., 63: 2113, 1914.
[18] J. A. M. A., 63: 2110, 1914.
[19] J. Urol., 4: 209, 1920.
[20] J. Urol., 47: 224, 1942.

Some of the cases in the first group show evidence of inflammatory changes and some do not. Bobbitt et al. believe these changes are due to the hemorrhagic extravasation from the thin-walled vessels. Payne and MacNider believe that the varicosed veins are themselves due to scarring in the cortico-medullary area caused by previous infection with impairment of venous drainage from the papilla. Bobbitt, Hoffman, and Werthammer attribute the formation of the varix to congenital weakness of the venous walls. If the assumption of Payne and MacNider is to be accepted, we wonder why the condition of renal varix is not commonly encountered in cases of pyelonephritis. Dr. Paul Kimmelsteil, pathologist at the Memorial Hospital, Charlotte, has suggested to us that the lesion in our first case and perhaps some of those reviewed in the literature be called a hamartoma.[21] Such a diagnosis would require no explanation for the cause or presence of the dilated veins, a hamartoma being defined[22] as the congenital over-development of some tissue element which belongs at the site at which it is found. He states that about a varix or angioma one would expect to have signs of compression of the tissues due to the growth or enlargement of the lesion. No such evidence could be demonstrated in our case. This area of compressed tissue has been noted in some cases reported in the literature and for this reason we must conclude that the first group of cases must include renal varix, angioma, and in our case perhaps hamartoma.

We have combined the second group of cases under a diagnosis of hemorrhagic papillitis for lack of better terminology. The signs of inflammation have varied from very acute in Quinby's first case to chronic in our case. The 3 cases accurately reported in the literature and our own case all had negative urine cultures. Of the 12 odd cases merely mentioned in discussions some were said to have had pus and sometimes colon bacilli in the urine. We wonder whether we may be dealing with several different pathological processes. In Quinby's first case Goodpasture conceived that the injury of the vessel walls might be due to some "circulating injurious agent." In Quinby's second case Goodpasture felt that the lesions could be explained by the presence of bacteria or a "local injurious agent." However, tissue cultures were negative in both cases. We have been able to offer no explanation to ourselves other than that these lesions may perhaps be due to some organism which we have been unable to demonstrate due to ignorance of its nature. Only future study can prove or abolish this postulate. A number of the cases included in this group seem to be cases of frank papillitis or pyelitis due to the colon bacillus with ulceration into a sizable vessel with resultant severe hemorrhage.

TREATMENT

We are convinced that nephrectomy is the treatment of choice in these cases where the bleeding is unilateral, persistent, and of a serious nature, granted that attempts have been made to stop the bleeding by instillation of caustics such as one per cent silver nitrate into the kidney pelvis, by administration of vitamin K, and perhaps x-ray therapy. Some authors believe that this practice may be dangerous, however, in that the bleeding of early malignancies may respond to this treatment and be disregarded. If this treatment is used, the patient should be followed by periodic pyelography with malignancy in mind. Various types of nephrotomy, from a small incision where a finger is introduced, to pole to pole deep incision, have been used by many of the reporting authors and frequently with success. We believe, however, that the risk of overlooking early malignancy is a ponderable one in such a procedure. Papillectomy in cases where the offending papilla is visualized may be considered by many as a satisfactory procedure. However, in a number of reported cases more than one papilla is involved and one may be easily overlooked, inasmuch as visualization of all the papillae requires not only a complete midline incision but assessory incisions up many of the calyces. Secondary hemorrhage is also a risk to be considered in this procedure, and MacGowan who performed three papillectomies strongly recommends nephrectomy as a safer procedure. We believe, therefore, that nephrotomy and papillectomy are inadequate and do not recommend them. One must always consider the opposite kidney, however, and where there is some lesion causing impaired function, all kidney tissue must be assiduously conserved.

---

[21] Personal communication.

[22] Karsner: Human Pathology. Philadelphia: J. B. Lippincott Co., 1935.

SUMMARY

We have presented the case histories of 2 patients on whom we were compelled to perform nephrectomy because of severe intractible unilateral hematuria, the cause of which we were unable to determine prior to postoperative examination of the kidneys.

Similar cases reported in the literature were reviewed and summarized and these cases discussed together with our 2 cases.

We arrived at the conclusion that these cases may be generally grouped under 2 headings: 1) vascular irregularities of the papilla, including varix, angioma, and hamartoma; and 2) hemorrhagic papillitis, the etiology of which we were unable to demonstrate. It was postulated that the latter group might be due to some organism which we and other authors have been unable to culture because of ignorance of its nature.

The treatment of these lesions was discussed and nephrectomy recommended in cases where conservative treatment fails to control the bleeding. Nephrotomy and papillectomy were condemned as inadequate procedures.

We are indebted to Dr. Paul Kimmelsteil and The Heineman Foundation for the preparation of the photographs and photomicrographs and to Mr. Rufus Meigs for reproduction of the roentgenograms.

1400 Scott Ave., Charlotte, N. C.

The Journal of Urology
Vol 61 No 1 January 1949
Printed in U S A

KIDNEY SUSPENSION BY USE OF FASCIA LATA

J E STRODE

From the Clinic, Honolulu, T H

In a previous publication, a method of suspending a prolapsed kidney by the use of fascia lata was described During the 16 year period since, this method has been used in 34 instances and has given such satisfactory results that it is felt that again calling attention to the procedure is justified

It must be realized that no method of kidney suspension will meet with good results unless cases are carefully selected so that one is sure beyond reasonable doubt that the symptoms complained of are the result of the malplaced kidney Individuals with generalized visceroptosis with a multitude of symptoms of more or less equal severity are not candidates for this operation

If the patient insists that there is pain in the region of the kidney or along the course of the ureter almost invariably on the right side and that the pain is more severe after being on her feet all day, that there have been recurrent attacks of urinary infection frequently associated with chills, fever and pain in the right flank, and particularly if the patient has had previous appendectomy, pelvic laparotomy or gallbladder removal without relief of symptoms and if intravenous pyelograms show a marked ptosis of the kidney when the patient is in the erect position, usually with some degree of hydronephrosis, then kidney suspension is indicated, and there is little doubt that the result will almost certainly be gratifying

The classical picture just presented cannot be insisted upon since there are other individuals who will be equally benefited who do not exhibit all the cardinal indications One cannot lay down hard and fast rules to follow but in general the finding of a ptotic kidney is no indication for surgery unless accompanied by symptoms very definitely pointing to this organ as the offender

The technique of the operation is so simple and easily carried out that a detailed description seems unnecessary A kidney incision large enough to adequately expose the ureter, particularly in its upper half, is all that is necessary Aberrant vessels or strands of fibrous tissue that may obstruct the ureter are dealt with in the usual manner No difficulty in exposing the kidney is encountered due to its mobility If one is in doubt about any intra-abdominal organ being productive of symptoms, it is easy to open the peritoneum and explore the abdomen We have explored the abdomen and removed the appendix on several occasions through this incision but so far we have not found an appendix that we thought was producing symptoms

A strip of fascia lata about 20 cm in length and 1 cm wide is obtained (fig 1) It is woven in and out of the capsule of the lower pole of the kidney (fig 2), being careful to see that it does not come near the pelvis where it might subsequently cause trouble A few interrupted sutures of cotton or silk, passed through the kidney capsule and through the fascia after it has been placed, may seem indicated to help hold it in place. The ends of the fascia are brought through the muscles above the incision as shown or may be looped over the last rib, if thought desirable. The ends of the fascia are overlapped and sutured with nonabsorbable suture material being shortened to the point where the kidney is brought into the most desirable position. No further effort to suspend the kidney is necessary. With the present tendency to early ambulation, the patient may be up and around the next day. The old practice of keeping these patients in bed for several weeks with the foot of the bed elevated is entirely unnecessary.

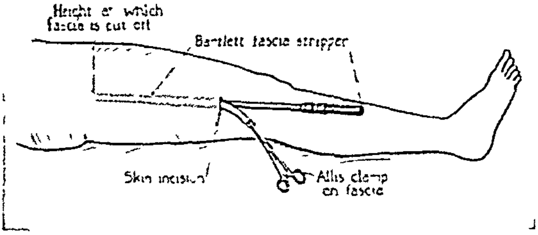


FIG. 1

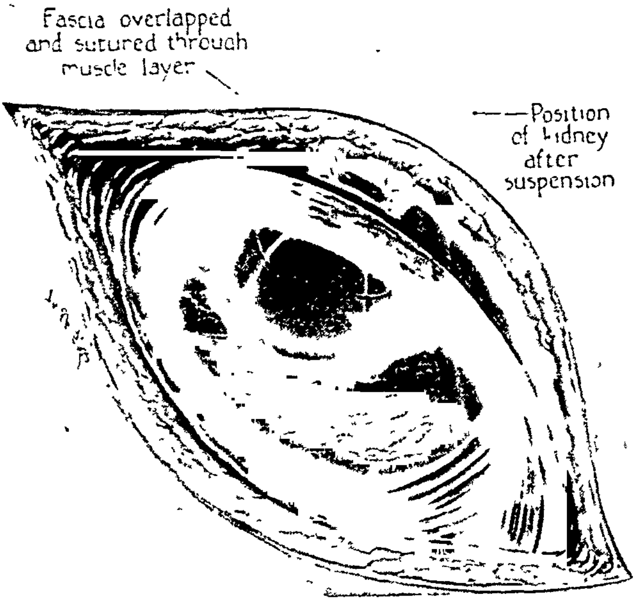

Fascia overlapped and sutured through muscle layer
Position of kidney after suspension

FIG. 2

Patients have been followed by use of intravenous urograms since the operation was first done in 1931, and no recurrence of the ptosis has been found.

The following case reports are examples to show what we believe are indications for this operation. Preoperative and postoperative intravenous pyelograms are included.

CASE REPORTS

Case 1. Mrs. P. H., a 34 year old Caucasian woman, was first treated for urinary infection in September 1933. Cystoscopic examination with catheterization of the ureters showed albumin, pus and B coli in culture in quantities from the right kidney Urine from the left kidney was normal Recurring attacks of pain and tenderness in the right kidney region with pus in the urine occurred over a period of 2 years Intravenous pyelograms showed ptosis of the right kidney with hydronephrosis and kinking of the upper ureter (fig 3, *A*) Attempts at relief of symptoms by the use of a kidney belt proved unsuccessful. The right kidney was suspended on September 10, 1935 Since operation, no recurrence of urinary infection has taken place and now, 12 years later, the patient says that the operation has been eminently successful

Case 2 Miss C T, a Japanese woman, aged 27, complained of intermittent backache and discomfort in the right side of the abdomen and right lower quadrant for the past 3 years The right kidney was easily palpable and freely movable Pelvic examination was negative Intravenous pyelograms showed some hydronephrosis of the right kidney with considerable ptosis and kinking of the upper ureter (fig 3, *B*)

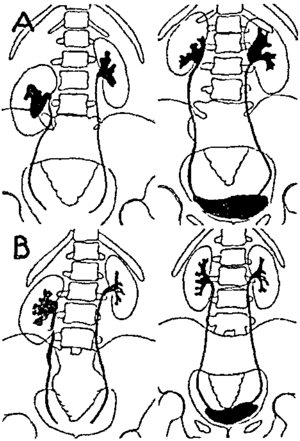


Fig 3 *A*, case 1 (Left) preoperative intravenous urogram, August 24, 1935 (Right) postoperative intravenous urogram, June 29, 1940
B, case 2 (Left) preoperative intravenous urogram, September 18, 1941 (Right) postoperative intravenous urogram, September 1, 1943

The right kidney was suspended on November 4, 1941 and at the same time the peritoneum in the anterior part of the incision was opened and a small fibrotic appendix removed Intravenous urograms 2 years later showed the right kidney in good position with no kinking of the ureter The patient has been relieved of the symptoms

Case 3 Mrs P. W., a 28 year old Caucasian woman, gave a history of urgency, frequency and burning on urination at intervals for the past 2 years *Intravenous urograms* on February 25, 1935 showed definite hydronephrosis on the right with considerable prolapse of the kidney The urine at this time dicated to help hold it in place. The ends of the fascia are brought through the muscles above the incision as shown or may be looped over the last rib, if thought desirable. The ends of the fascia are overlapped and sutured with nonabsorbable suture material being shortened to the point where the kidney is brought into the most desirable position. No further effort to suspend the kidney is necessary. With the present tendency to early ambulation, the patient may be up and around the next day. The old practice of keeping these patients in bed for several weeks with the foot of the bed elevated is entirely unnecessary.

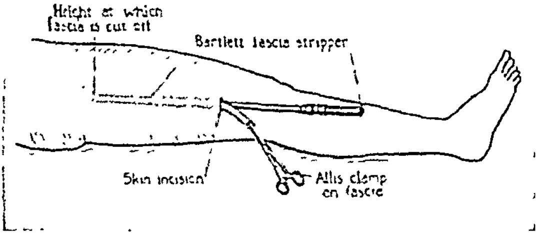


Fig. 1

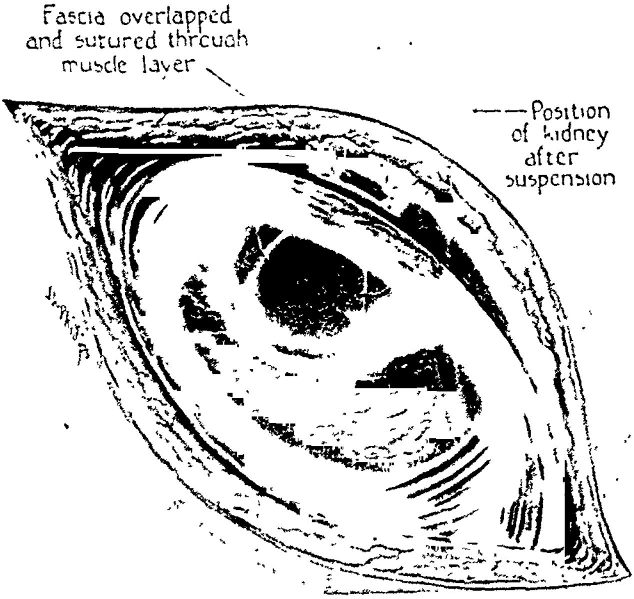

Fascia overlapped and sutured through muscle layer
Position of kidney after suspension

Fig. 2

Patients have been followed by use of intravenous urograms since the operation was first done in 1931, and no recurrence of the ptosis has been found.

The following case reports are examples to show what we believe are indications for this operation. Preoperative and postoperative intravenous pyelograms are included.

CASE REPORTS

Case 1. Mrs. P. H., a 34 year old Caucasian woman, was first treated for urinary infection in September 1933. Cystoscopic examination with catheteriza-

The patient has been relieved of her previous symptoms

Case 5 Miss B S , a 16 year old girl, was first seen on April 7, 1937, complaining of indefinite abdominal pain without localization

Urine examination was negative Intravenous urograms on December 12, 1938 showed good filling of the right kidney with considerable ptosis in the erect position There was no evidence of a kidney on the left and cystoscopy revealed no evidence of a ureteral orifice

The patient was seen repeatedly for this indefinite abdominal pain over a period of 10 years All examinations, including gastro-intestinal study, were negative In March 1947, the patient developed frequency of urination, burning and pain with discomfort in the right loin which was more severe when standing and relieved by lying down The urine contained much pus The right kidney was easily palpable and repeat intravenous urograms showed more marked ptosis than previously, with early hydronephrosis (fig 5, *A*) It was deemed advisable to suspend the right kidney and this was done on April 1, 1947 Ten weeks later, intravenous urograms showed the kidney in good position and the patient was free of symptoms

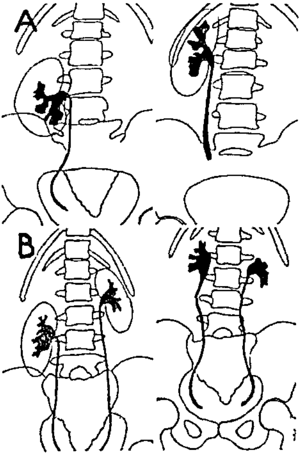


FIG 5 *A*, case 5 (Left) preoperative intravenous urogram, March 13, 1947 (Right) postoperative intravenous urogram June 23, 1947
B, case 6 (Left) preoperative intravenous urogram, January 9, 1935 (Right) postoperative intravenous urogram May 10, 1940

Case 6 Miss G , a 20 year old Caucasian woman, was first seen in December 1934, with a history of recurring attacks of pain and tenderness in the right side of the abdomen and the right kidney region associated with frequency and burning on urination, generally lasting for 3 or 4 days

On examination, the right kidney was easily palpable, enlarged and tender Cystoscopy with examination of urine from each kidney revealed nothing abshowed 3 plus white blood cells in clumps. On March 4, 1934, cystoscopic examination with ureteral catheterization showed very little abnormal in the bladder and kidney urine specimens. Cultures from each were sterile. The preoperative intravenous urogram is shown in figure 4, *A*. A kidney suspension was done on March 7, 1938 and the patient made an uneventful recovery. Intravenous pyelograms on April 9, 1938 showed the right kidney in good position with less hydronephrosis.

In November 1940, the patient came in complaining of discomfort especially in the right kidney area, less in the left. Intravenous urograms showed some kinking of the right ureter below the renal pelvis and hydronephrosis but the position of the kidney was good (fig. 4, *A*). It was thought that postoperative adhesions probably accounted for this finding. On December 2, 1940, the right ureter was dilated under anesthesia and since this time the patient has been relieved of most of her symptoms, but she still has some discomfort in the right lumbar area in spite of good position of the kidney.

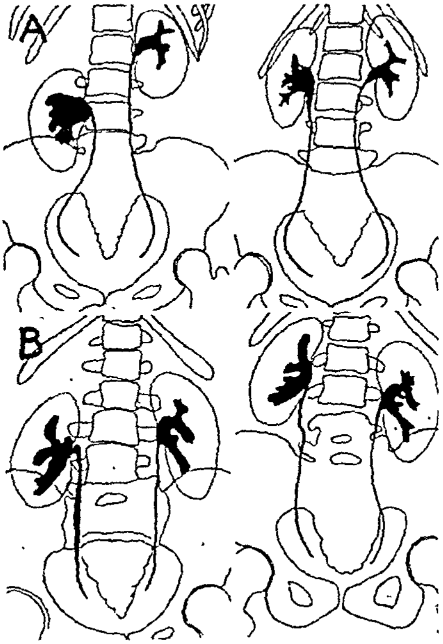


FIG. 4. *A*, case 3. (Left) preoperative intravenous urogram, February 1938. (Right) postoperative intravenous urogram, November 1940.
B, case 4. (Left) preoperative intravenous urogram, October 20, 1935. (Right) postoperative intravenous urogram, October 23, 1938.

Case 4. Miss S. C., a Caucasian woman, aged 35, complained of pain and discomfort of indefinite duration in the right side of the abdomen and the right lower quadrant. The pain had been more marked during the past 3 weeks. The right kidney was palpable and tender. The appendix had been removed previously.

Urinalysis was negative. Intravenous urograms showed ptosis of both kidneys, more on the right (fig. 4, *B*).

Renal suspension was done on November 4, 1938. The peritoneum was opened and the gallbladder and pelvis were explored and were negative.

normal The appendix looked innocuous but it was removed The pathological examination showed no evidence of inflammation

Intravenous pyelograms on March 8, 1943 showed the kidney in satisfactory position and she stated that she had been relieved of the symptoms for which she was operated upon

Case 8 Mrs E M, a Caucasian woman, aged 40, was first seen for pain in the right upper quadrant and back, in January 1935 During 13 months of observation she had frequent attacks of this pain associated with nausea but no vomiting There was some tenderness in the region of the gallbladder but on investigation this organ filled well and emptied normally Urine examinations were negative Pelvic examination was negative

Intravenous urography showed rather marked ptosis of the right kidney with some hydronephrosis (fig 6, *B*) At operation on June 26, 1936 the right kidney was found freely movable The kidney was suspended by fascia in the usual manner Subsequent x-ray studies 11 years after suspension showed the kidney in good position

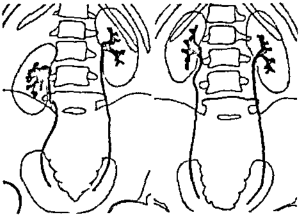


FIG 7 Case 9 (Left) preoperative intravenous urogram, August 1, 1942 (Right) postoperative intravenous urogram, October 5, 1944

This patient has been an employee of The Clinic before and since operation and has come under daily observation She states that she has been free of the symptoms above enumerated since the kidney was suspended

Case 9 Mrs T, a 24 year old Japanese woman, was first observed on July 31, 1944 She had had 3 previous pregnancies The history revealed that the patient had had intermittent attacks of pain in the right side and in the appendix region for the past 3 years On examination there was rather acute tenderness over the appendix region

The blood count showed 13,800 white cells and 62 per cent polymorphonuclear leucocytes The urine examination was negative Pelvic examination was negative The patient had been told previously that her trouble was due to a "floating kidney" Intravenous pyelograms showed considerable ptosis of the right kidney with moderate hydronephrosis (fig 7)

We were in doubt as to whether her symptoms were due to her appendix or to her kidney so decided to take care of both

Operation was performed on August 4, 1944 and the kidney was suspended by fascia in the usual manner The peritoneum was opened and the gallbladder and pelvic organs were explored and were negative The appendix did not appear to be causing trouble but it was removed. Microscopic examination showed no definite evidence of active inflammation. Intravenous pyelograms 3 months after operation showed the kidney in good position and the patient stated that she had been completely relieved of the pain which she had before.

DISCUSSION

A number of years ago, suspending prolapsed kidneys became quite a fad but fell into disrepute because of two reasons: 1) Proper selection of cases for the operation was not possible; 2) the method used in suspending the kidney was not adequate and many recurrences took place.

As pointed out at the beginning of this discussion, a few individuals will present a more or less clear-cut picture in which suspending the kidney will prove to be almost always successful while others will get an equally good result when the picture presented is less typical. The two most suggestive findings are pain in the right loin or right quadrant associated with recurring attacks of urinary infection. In thin individuals the kidney is palpable, easily moved about, and frequently tender. Undoubtedly, practically all symptoms produced by a ptotic kidney are due to urinary obstruction at or near the ureteropelvic junction. Rarely will suspending the kidney be indicated unless there is evidence of some degree of hydronephrosis.

Intravenous urography has been the greatest aid in substantiating or ruling out the clinical impression that the patient's symptoms are due to the malplaced kidney. Pictures of the kidneys and ureters made at 5, 10 and 15 minute intervals after intravenous injection of 20 cc of 35 per cent diodrast with the patient supine, and one after 20 minutes with the patient erect with no pressure on the abdomen, usually gives the desired information. Some individuals excrete the dye so rapidly that it may be necessary to take the erect picture earlier than 20 minutes to outline the pelvis and ureter adequately.

Trouble with the appendix comes up most frequently in the differential diagnosis and when this point remains uncertain, we have no hesitancy in opening the peritoneum and removing this organ at the time the kidney is suspended. The pelvis may also be explored if thought advisable and abnormalities dealt with at the time or subsequently, as indicated. Needless to say, adequate investigation of the gallbladder, gastro-intestinal tract and pelvis is made preoperatively as deemed indicated.

It has not seemed advisable to use fascia for suspension of the kidney when it was necessary to drain the region of the kidney, as, for instance, when a portion of the kidney was resected or, for any reason, the pelvis or ureter was opened, or when adequate circulation to a portion of the kidney seemed questionable. Transplanted fascia tolerates infection poorly.

Treating ptosis of the kidney, that is causing symptoms, conservatively, has in our experience been most unsatisfactory. It is difficult—almost impossible—to construct any appliance that will hold the kidney in place that does not cause the patient almost equally distressing symptoms from pressure. In the treatment of renal ptosis it has been our policy to be conservative for we believe relatively few of these cases should be subjected to surgery. During a 16 year period 34 cases were subjected to the operation under discussion, and it is believed that this indicates that we have been conservative. Two of the 34 cases occurred in men, and all but one on the right side. I know of no plausible explanation to explain these findings, unless it is due to the normally lower position of the kidney on the right because of the liver. Pregnancy does not seem to be a contributing factor.

Careful selection of patients with nephroptosis for operation and the use of fascia—obtained usually from the leg or occasionally from the kidney incision itself—have brought results that are most gratifying. It is by no means the only satisfactory way of suspending the kidney but in our hands it has been the *most* satisfactory.

REFERENCE

Strode, J. E.: Kidney suspension by use of fascia lata. J. Urol., 32: 171–175, 1934.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January, 1949
Printed in U.S.A.

REPORT OF POSTOPERATIVE SURVIVAL OF TWO CASES OF MALIGNANCY: 1) CARCINOMA OF THE ADRENAL CORTEX; 2) WILMS' TUMOR IN AN ADULT

MARTIN J. LOEB

From the Bronx Hospital, New York, N. Y.

In 1941 I reported a case of "Adrenal Carcinoma Without Endocrinological Symptoms" in the *Journal of Urology* (vol. 45, p. 785). Again, in 1943, I reported in the same journal (vol. 50, p. 268) "A Case of Wilms' Tumor in an Adult." It is the purpose of this paper to give a brief review of these cases and their current status. For complete reports, with illustrations, the reader is referred to the original papers.

CARCINOMA OF THE ADRENAL CORTEX

C. S., aged 57 years, had been ill 2 years. She was admitted to the Bronx Hospital November 11, 1939. The chief symptoms were loss of 40 pounds in weight, and weakness.

Cystoscopy, x-rays, and pyelograms revealed a normal left kidney. A large mass occupied the right side of the abdomen and displaced the kidney downward in the following manner: The outer border of the kidney faced downward and the upper pole outward. The pelvis of the kidney was directed upward, the kidney making a right angle with the spine. Perirenal insufflation disclosed a large mass which was not connected with the kidney.

The patient was operated on in November 1939 and an adrenal carcinoma, which weighed 1100 gm. was removed.

The microscopic report is as follows: There was a marked cellular tumor which was limited by a thick connective tissue capsule. Cellular components of tumor were essentially of small and large polymorphic, slightly eosinophilic or neutrophilic cells with distinctly granular cytoplasm. Nuclei were frequently markedly hyperchromatic, varied considerably in size and occasional multinucleated cell forms and evidence of active cell division are noted. Stroma was rather sparse but well vascularized. Tumor cells comprised solid masses which often were the seat of hemorrhagic necrosis. The cell outlines were indistinct, the individual elements blending imperceptibly with one another. No evidence of papillary structure or lumen formation was present. There was an occasional suggestion of perithelial arrangement. In general, cell structure was identical with that seen in adrenal cortex, although no clear zonal demarcation was evident.

The patient was subjected to radiation therapy, a total dose of 11,750 R. during a period of about 4 months. The treatment was applied anteriorly, posteriorly and laterally.

The patient on admission to the hospital weighed 142 pounds; after operation, 134 pounds. Subsequent to that, she gained weight and gradually improved.

The patient was examined in my office on November 1, 1948. X-ray examination of the chest, skull and long bones revealed no abnormalities. The patient's general condition was good except that she was obese. Her height was 5 feet, 1 inch; her weight 175 pounds; her weight today is about the same as in 1937 at which time her symptoms of loss of weight and general weakness began. Her blood pressure was 140/80. The blood chemistry was slightly elevated. The blood count is normal.

The condition of the patient today, 9 years after operation and postoperative radiation, is excellent. She is able to attend to her work and take care of her family. Since she belongs to a low income group, the entire household burden rests upon her.

WILMS' TUMOR IN AN ADULT

F. A., a 49 year old housewife, was admitted to the hospital in November 1941. Apparently she had some symptoms referable to the right lumbar region for about 1 year. About a week before admission, the patient suddenly began to have severe pains in the right lumbar region. These pains were sharp and constant. The pains radiated to the front of the abdomen and inguinal region. At the same time urgency and frequency manifested themselves and later on, inability to void. Bloody urine was obtained by catheterization, after which she was able to void. The inability to urinate was caused by obstruction from a clot which formed in the bladder.

Cystoscopic examination revealed old bloody urine in the bladder. Catheters were inserted into the ureters. On the left side the catheter reached to the pelvis of the kidney and on the right side to about 4 cm. below the ureteropelvic junction. Bloody urine was obtained from the right side. The blood was old. There was no function on the right side. There was good function on the left side. Indigo carmine returned from the left side within 5 minutes; none from the right side. Bilateral pyelograms were done. The urine obtained from the right kidney was too bloody to be examined. The culture showed growth of staphylococci.

The pyelogram on the left side showed normal filling of the pelvis and calyces. On the right side there was gross enlargement of the kidney shadow over its upper pole with elongation and distortion of the superior calyces. A communicating area was also filled with contrast medium. These findings indicated a cystic mass in the upper pole of the right kidney.

The pre-operative diagnosis was carcinoma of the kidney.

A right nephrectomy was done November 11, 1941.

Radiation treatment was subsequently given by Dr. J. Freid at his office. She received a total dosage of 4200 R.

One microscopic section exhibited characteristic cellular morphology of this tumor. It was a cellular neoplasm consisting chiefly of spindle cells. These cells ran in various directions but in some areas had a distinctly unidirectional character. Some of the cells were polyhedral, varying in shape from oval to round with a rather vesicular nucleus. Scattered cells displayed definite hyperchromatism. The general appearance was that of a sarcoma of spindle cell variety with interspersed areas of what appeared to be definitely smooth muscle

   A. Tumor projecting from ureteral orifice in about 25 per cent.
   B. Bulge in ureteral ridge.
   C. Edema and congestion of ureteral orifice.
   D. *Trickle of blood from orifice after vaginal* or *rectal manipulation.*
   E. Obstruction, either complete, or a mushy resiliency on attempted passage of catheter.
   F. Decrease in function on involved side.

8) Roentgenographic studies may reveal:
   A. Hydronephrosis on affected side.
   B. Goblet shaped filling defect in region of tumor.
   C. Metastases in bones or chest.

9) Treatment: Treatment of choice is extraperitoneal nephro-ureterectomy with segmental resection of bladder. If necessary to do operation in 2 stages, remove tumor at first operation. Be certain tumor is malignant (frozen section if in doubt) before radical resection is done. Pre- and postoperative radiation probably of little value.

10) Pathology: There is great confusion over nomenclature but probably 60 per cent of the tumors are papillary and 40 per cent are solid carcinomata.

11) Metastases: 34 per cent. Most frequent sites are retroperitoneal lymph nodes, liver, bones, and lungs.

12) Results: Confusing because of inadequate follow-up.
   A. Postoperative deaths, about 25 per cent.
   B. No patient living more than 4 years postoperative died of metastases.
   C. *Of 40 patients reported* well *only* 14 were *followed 4 or more years.* One case was well 13 years; one, 12; one, 11; one, 9; two, 8; two, 7; and one, 6 years after operation.

13) Follow-up: The patient should be examined every 3 months the first year after operation, every 6 months the second, third and fourth years, and yearly thereafter. The examination should consist of a general physical examination, pelvic or rectal examination, cystoscopic examination, and x-ray of lumbar spine and pelvis.

CASE REPORT

An unmarried 61 year old woman was first seen in consultation on May 12, 1941, complaining of hematuria. She had never had any urinary complaints until the sudden appearance 24 hours previously of painless, gross hematuria which had persisted, and was unaccompanied by other urinary symptoms. The past history was relatively unimportant. There had never been any urinary disturbances. The menstrual periods had ceased in about 1920 after a normal menstrual life. She had had moderately advanced hypertension for 30 years, but had never had symptoms from it. The physical examination was essentially normal. The patient was moderately obese. The blood pressure was 200/100. There was no abdominal or costovertebral angle tenderness and no masses. Rectal examination revealed no abnormalities. The catheterized urine was grossly bloody; the culture was sterile. The 2 hour phenolsulphonphthalein function test revealed only 50 per cent excretion. The excretion curve showed 15, 10, 10 and 15 per cent in 15, 30, 60 and 120 minutes. The blood nonprotein nitrogen was 32 mg. per cent.

An intravenous urogram taken on May 13, 1941, showed a normal right, and an imperfectly filled left kidney The ureters were not visualized.

Cystoscopic examination on May 14, 1941 revealed grossly bloody urine and a normal bladder. Neither urine nor blood was seen emerging from either ureteral orifice. The left orifice was catheterized with a No. 7 pointed tip catheter. Mild obstruction was encountered just inside the ureteral orifice and the catheter passed all the way up the ureter with some difficulty. Clear urine drained from the catheter, a culture of which was negative. A plain x-ray was normal. A pyelo-ureterogram using 37 cc of opaque medium showed a large hydronephrosis with dilated, blunted calyces. The ureter was moderately dilated to a point just above the bladder where there was an acute narrowing for a few centimeters, then a moderately dilated area below this (fig. 1). A diagnosis of ureteral tumor was made. There was no gross hematuria after this examination.

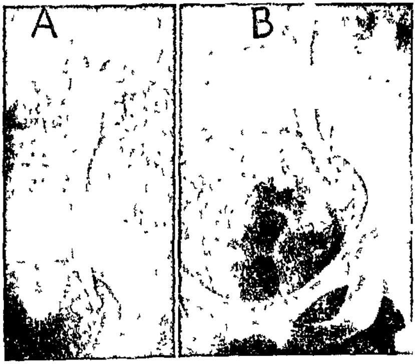


FIG 1

On May 23, and June 3, 1941 attempts were made to catheterize the left ureteral orifice to obtain a differential phenolsulphonphthalein function test, but each time the tip of the catheter obstructed 1–2 cm. inside the orifice and did not drain.

It was thought that there was enough evidence of a ureteral tumor to warrant an exploratory operation. On June 10, 1941 the lower ureter was explored through a left gridiron, extraperitoneal incision The ureter was normal as it emerged from the bladder. Approximately 1.0 cm. above this point the ureter became dilated and for about 5.0 cm. was filled with a solid tumor. There was no evidence of extension of the tumor through the ureteral wall Above the tumor area the ureter became dilated and thin walled, and the lumen was free of palpable tumor mass. The ureter was resected from the bladder with a small margin of bladder wall; then freed upward to the kidney. The kidney was

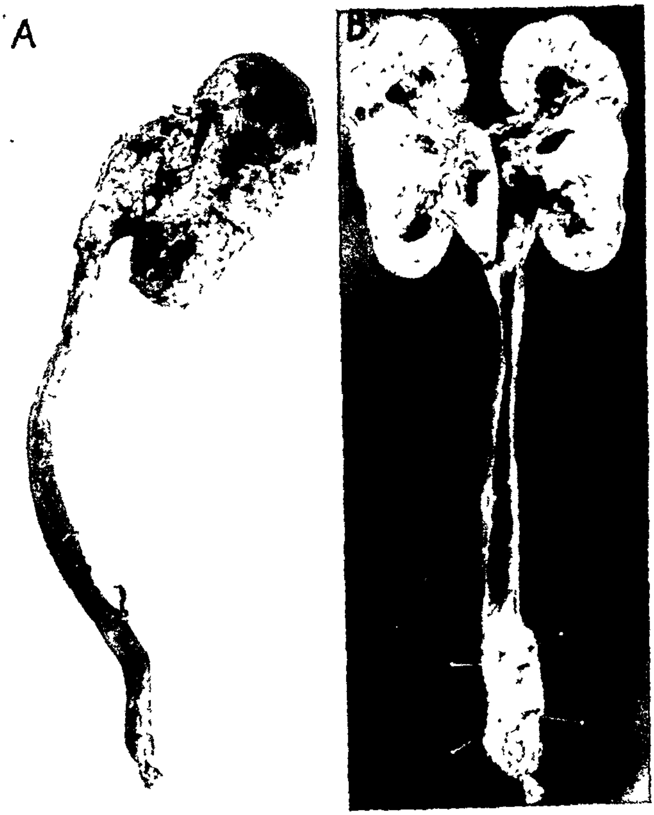


FIG. 2

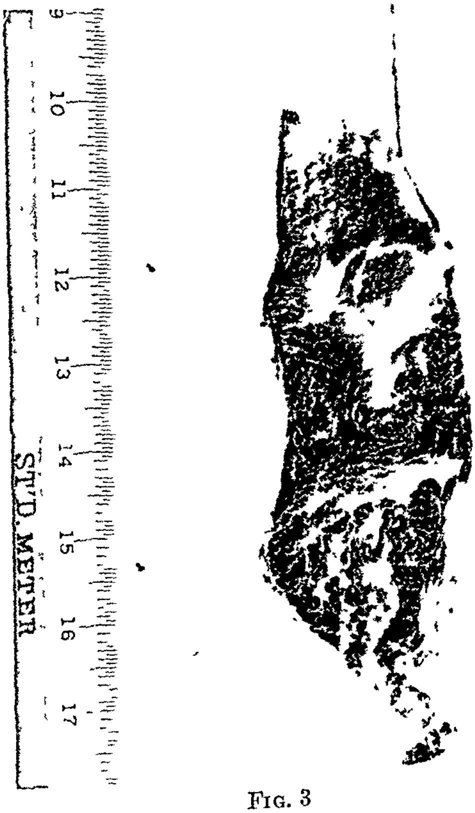


FIG. 3

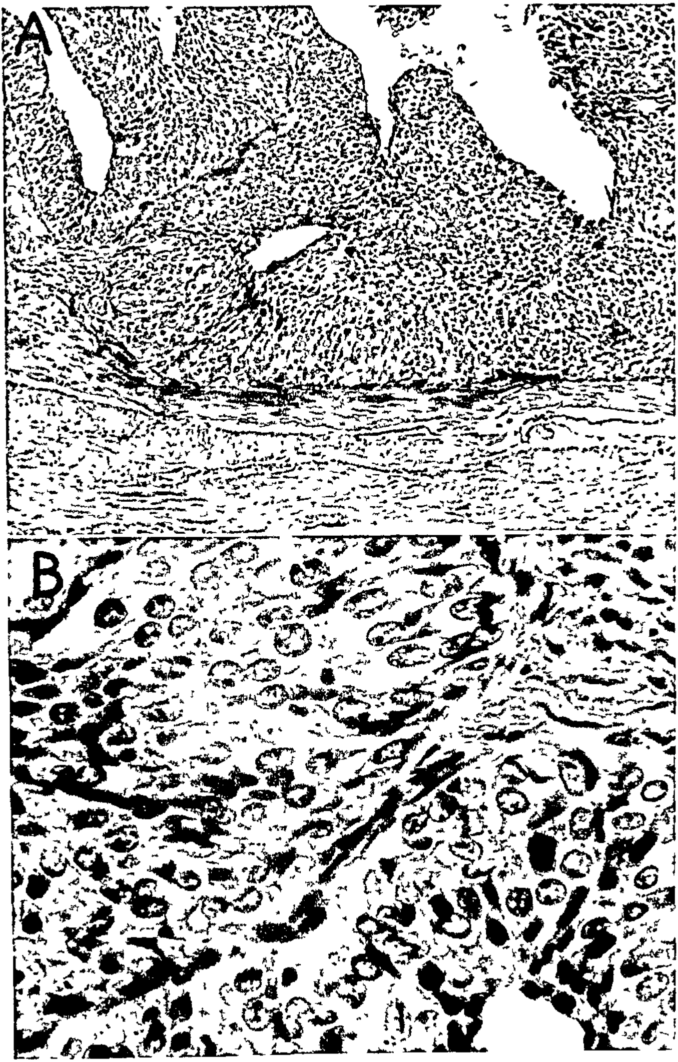


FIG 4

only slightly enlarged; the dilated pelvis was extrarenal, and the kidney pedicle was unusually long. After the kidney was freed by blunt dissection it was brought down into the gridiron incision so that the pedicle was exposed, clamped, ligated, and cut, and the entire kidney and ureter removed. The postoperative course was uneventful. The blood pressure fell to near normal after the operation, but as soon as the patient became ambulatory it rose to the former level, where it has remained since. It has not increased since the operation, however.

The gross specimen revealed the tumor mass occupying a space of about 5.0 cm. in the lower ureter. The ureter was about 2.0 cm. in diameter at this point and above this area was dilated and thin walled, but the mucosa above the tumor was normal. The kidney pelvis was dilated. The renal substance showed some scarring. Microscopic sections of the tumor showed a papillary carcinoma. Numerous sections through the tumor revealed no invasion of the ureteral wall (figs. 2, 3, 4).

For the first year following the operation the patient was examined every 3 months, and the next 2 years at 6 month intervals. The last examination, until recently, was 4 years after the operation. The last examination was on February 28, 1948. There has been no evidence of recurrence of the tumor as evidenced by abdominal mass, pelvic mass or induration, and cystoscopic examination has revealed a normal bladder.

In conclusion, a case of primary carcinoma of the ureter has been presented. The preoperative x-ray findings suggested a ureteral tumor. At the time of operation there was no gross evidence of extension or metastases. The entire ureter and kidney were removed through an extraperitoneal lower gridiron incision. The patient has remained well and has had no evidence of recurrence of the carcinoma after being followed 6 years and 10 months.

SUMMARY

A case of primary carcinoma of the ureter has been presented. It is unusual in only one respect. The patient has been followed closely for nearly 7 years after the original operation and is alive and well, with no evidence of recurrence. This is the tenth case that has been followed more than 6 years. The literature on the condition has been reviewed and summarized and the bibliography is brought up to date.

11 East Chase St., Baltimore 2, Md.

REFERENCES

Bowie, C. F. and Bors, E.: J. Urol., 54: 434, 1945.
Caraven, J.: J. d'urol., 52: 11, 1944.
Case Report: New Eng. J. Med.: 235: 337, 1946.
Counseller, V. S., Cook, E. N. and Seefield, P. H.: J. Urol., 51: 606, 1944.
De La Peña, A. and De La Peña, E.: Urol. and Cutan. Rev., 50: 667, 1946.
Gualtieri, T., Hayes, J. and Segal, A., J. Urol., 59: 1083, 1948.
Hundley, J. M. and Hunter, J. S., J. Urol., 58: 176, 1947.
Jaffe, S. A. and Mendillo, A. J.: Am. J. Surg., 62: 126, 1943.
Lazarus, J. A. and Marks, M. S.: J. Urol., 54: 140, 1945.
Lepoutre, C.: J. d'urol., 52: 143, 1944–45.
McClelland, J. C.: J. Urol., 52: 522, 1944.
Regan, J. R.: J. Urol., 50: 304, 1943.
Scott, W. W.: J. Urol., 50: 45, 1943.
Van Gulik, F. H.: Nederl. tijdschr. v. geneesk., 90: 503, 1946.
Vest, S. A.: J. Urol., 53: 97, 1945.

THE JOURNAL OF UROLOGY
Vol 61, No 1, January 1949
Printed in U S A

CARCINOMA OF THE URETER. REPORT OF THREE CASES[1]

W H BROOKS

In view of the relative rarity of primary tumors of the ureter, 3 cases of primary carcinoma are here reported

CASE REPORTS

Case 1 G V R , a locomotive engineer, aged 48, was admitted to St Luke's Hospital on November 8, 1941 after suffering for 24 hours intermittent attacks of colicky pain in the right flank radiating anteriorly and downward toward the urinary bladder A diagnosis of right ureteral calculus was made, and I was asked to see the patient

On cystoscopic examination no urine came from the right ureter and none could be aspirated from the ureteral catheter owing to an obstruction about 4 cm inside the right ureteral orifice Bilateral pyelograms demonstrated a small stone, with the tip of the catheter lying above it, in the lower portion of the right ureter, there was evidence of extravasation of the skiodan solution into the periureteral tissues with no dye in the right ureter or pelvis (fig 1) A diagnosis was made of impacted calculus in and perforation of the lower portion of the right ureter

At operation, the ureter was dilated about 3 times normal size, and great edema and inflammation of the periureteral tissues were present There was a tear in the ureter 2 inches above the ureterovesical junction with moderate extravasation of urine Because of this rupture and an impacted calculus at the right ureterovesical junction, *which could not be removed because of the inflammatory* and friable condition of the ureter, ureterocutaneous anastomosis was performed

The patient, greatly depressed over the ureterostomy, elected nephrectomy Twelve days after the first operation, nephro-ureterectomy was accomplished in 1 stage, and papillary carcinoma of the upper segment of the ureter was discovered on pathologic examination

The pathologic report, made by Dr Lucien Y Dyrenforth, follows "The specimen is a soft, discolored, enlarged kidney with a dilated, edematous ureter Dilatation of the superior calix, focal areas of abscess and necrosis, a generalized intense swelling throughout the kidney, arteriosclerotic changes in the renal vascular system and glomerular tufts are noted A new growth arises from the lining epithelium of the upper portion of the ureter about 1 inch below the ureteropelvic junction and extends beneath the mucosa It forms rosettes and papillary patterns of spindle shaped epithelioid cells (fig 2) Atypical staining and mitotic figures are present Various sections show that it is confined to a short space in the upper third of the ureter Diagnosis Papillary carcinoma of the ureter, chronic and subacute pyelonephritis, suppurative pyelitis and nephrosclerosis "

---

[1] Read at annual meeting, Southeastern Section, American Urological Association, Hollywood, Fla , January 9, 1948

The patient made an uneventful recovery and was discharged from the hospital on December 8. During the 6 years that have elapsed since that time, repeated examinations have given negative results, and he has continued his railroad work.

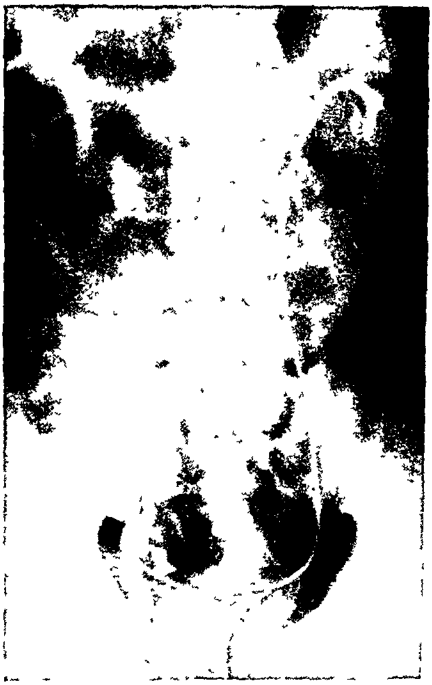


FIG. 1. Case 1. Retrograde pyelogram showing small calculus in lower segment of right ureter and extravasation of contrast medium outside ureter.

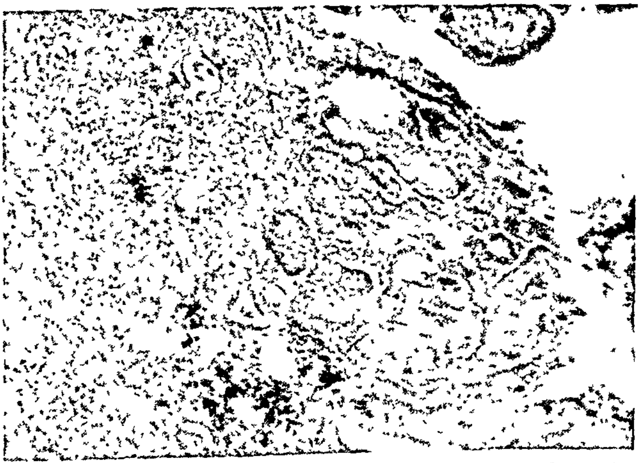


FIG. 2. Case 1. Low power photomicrograph of epithelial neoplasm from upper portion of ureter. Diagnosis: Papillary carcinoma.

Case 2. H. S. W., a man aged 59, was admitted to St. Luke's Hospital on August 29, 1947. On two successive nights, 10 days prior to admission, he had had a chill followed by temperature of 103 to 104 F., and elevation of temperature to approximately 103 F. had continued daily since that time. His family physician had given him 300,000 units of penicillin daily along with sulfa drugs for 6 days immediately preceding hospitalization, and his only complaint had been feeling tired when the temperature was elevated. Five weeks previously he had undergone repair of bilateral inguinal hernia, with catheterization the first night postoperatively, and had been discharged from the hospital 14 days after the herniorrhaphy.

On admission, the temperature was 103.4 F., and there was a 1 to 2 plus prostatic enlargement. The urine contained 10 to 15 white blood cells and 1 to 3 red blood cells per high power field. The prostatic smear showed an occasional white blood cell. The blood count was red cells 3.6 million with hemoglobin 68 per cent (11.5 gm.), white cells 41,150, stab forms 6, segmented forms 90, lymphocytes 3 and monocytes 1. With symptomatic treatment, the temperature returned to normal by lysis on the fifth day of hospitalization.

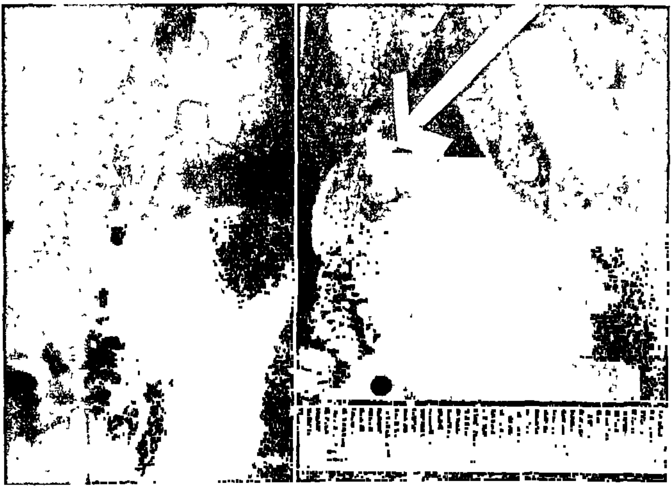


Fig. 3. Case 2. *A*, Retrograde pyelo-ureterogram showing moderate hydronephrosis and filling defect in upper segment of ureter. *B*, Showing details of growth appearing as a firm white mass on lower margin of ureteral defect.

On September 3, indigo carmine appeared from the right ureteral orifice in 4 minutes after injection intravenously in 4 plus concentration and from the left ureteral orifice 5 minutes after injection in 3 plus concentration. A No. 6 ureteral catheter was passed up each ureter without difficulty, and from the one on the left, after it had passed 20 cm., a hydronephrotic drip was obtained and 50 cc. of grossly clear urine was aspirated from the left renal pelvis.

Retrograde pyelograms revealed a filling defect in the left ureter (fig. 3, *A*) about 2 cm. long and approximately 2 inches below the ureteropelvic junction with moderate dilatation of the ureter and renal pelvis above it. The next day, intravenous pyelograms likewise showed moderate dilatation of the left renal pelvis and upper portion of the ureter. A diagnosis of tumor of the left ureter was made.

On September 10, nephrectomy and partial ureterectomy were performed. A small abscess about 2 inches below the ureteropelvic junction with necrotic ureteral wall and surrounding inflammatory area was present. At the lower margin of the abscess cavity a golden yellow new growth about ½ cm. by ¼ cm. in diameter apparently arose from the mucosa of the ureter. It was attached to and had extensively invaded the ureteral wall.

The pathologic report was as follows: "The specimen consists of a kidney with 8 cm. of ureter attached. There is a rupture of the ureter 4 cm. below the renal pelvis (fig. 3, *B*). The outer layers of the ureter at this point are covered by fibrous and granulation tissue. A yellow mass in the wall of the ureter measures 0.3 cm. in diameter. Beneath this mass there is a papilloma in the mucosa also measuring 0.3 *cm. in diameter.* There is a redundancy of the epithelial lining of the ureter below the ureteropelvic junction. Dense scirrhous proliferation and thickening of the supporting connective tissue are present (fig. 4). The mucous membrane is redundant and contains darkly stained cells ranging from spindle to round form. There is a group of these cells within the sclerotic matrix. Response of granulation tissue to inflammation in the mucous membrane is pronounced. Diagnosis: Scirrhous carcinoma of the wall of the ureter."

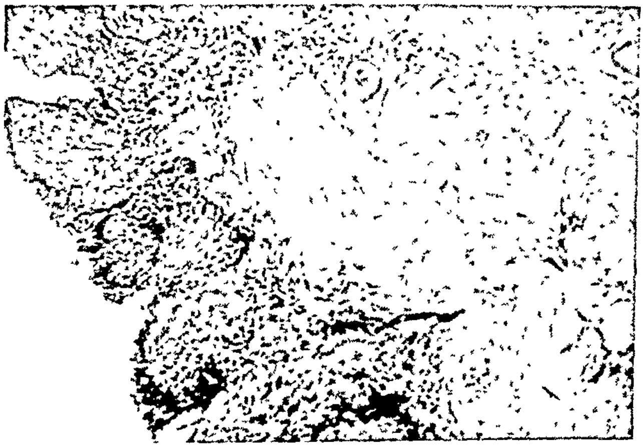


FIG. 4. Case 2. Low power photomicrograph showing transitional type of epithelium comprising tumor. Extension of cell groups into dense matrix is seen where break occurs in basement membrane.

High voltage roentgen therapy was instituted postoperatively, and follow-up cystoscopic studies have been carried out. There has been no evidence of recurrence up to the present time.

Case 3. R. T., male, aged 51, was referred on August 9, 1947 because of painless hematuria of 24 hours' duration. There had been occasional sharp pain in the left flank and left lower quadrant of the abdomen for 2 months and pain intermittently in the lower part of the back for 3 years.

On physical examination, slight tenderness to jar percussion was noted over the left renal area. There was grossly bloody urine. The blood count was red cells 4.13 million with hemoglobin 68 per cent (11.5 gm.), white cells 4,300, polymorphonuclears 56 per cent and lymphocytes 44 per cent.

Two days after admission, on cystoscopic examination, pink urine dribbled from the left ureter in small amounts at intervals. Indigo carmine, injected intravenously, appeared from the right ureteral orifice 6 minutes after injection in 4 plus concentration; no dye appeared from the left ureter in 15 minutes. A No. 5 ureteral catheter was passed up each ureter easily. Grossly bloody urine drained from the left catheter. Bilateral retrograde pyelo-ureterograms revealed duplication of the renal pelvis and upper portion of the ureter on the right side. On the left side there was slight but definite hydronephrosis. The left ureter was dilated 1 cm. in its lower third from the level of the sacrum to just below the promontory of the sacrum where the dilatation ended abruptly. It was thought at this time that the dilatation and obstruction in the lower portion of the left ureter might be due to an accumulation there of blood clots.

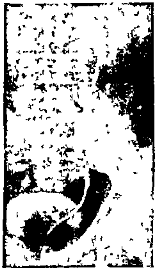


FIG. 5. Case 3. Retrograde pyelo-ureterogram showing filling defect at junction of lower and middle thirds of left ureter

On August 15, four days after the first examination, cystoscopy revealed grossly clear urine in the bladder. After a catheter was passed up the left ureter for a distance of 7 cm. grossly clear urine was obtained. A left ureterogram demonstrated a rounded, 1 cm. filling defect in the left ureter at a point about 2 cm. above the brim of the bony pelvis. The ureter and renal pelvis above were entirely normal in appearance.

On August 20, the patient had a chill and there were signs of infection of the upper portion of the urinary tract on the left side (fig. 5). Two days later the blood urea was 41.3 mg. per hundred cubic centimeters of blood. A ureteral catheter, from which a hydronephrotic drip was obtained at 7 cm. up the left ureter, was fixed in place as a retention catheter. Sulfadiazine was administered and on August 25 the temperature returned to normal. A ureterogram at this time again demonstrated the filling defect in the lower portion of the left ureter. Since this finding remained constant, a diagnosis of primary tumor of the lower segment of the left ureter was made.

The next day nephro-ureterectomy was performed. About 2 inches above the

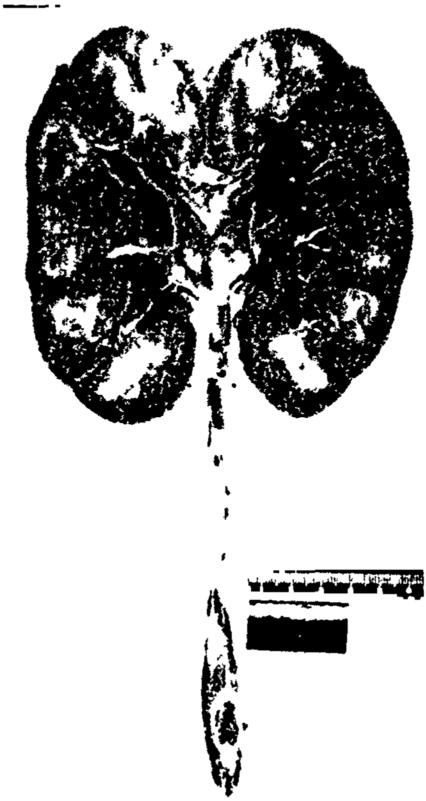
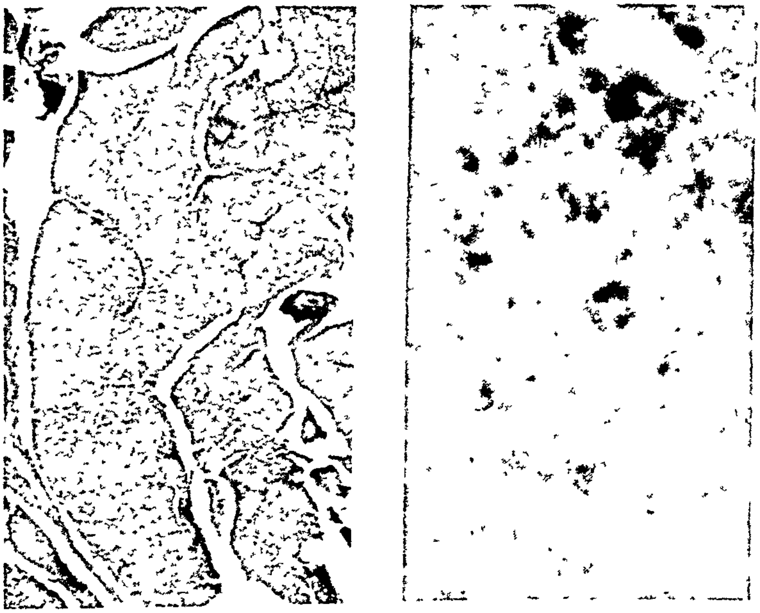


FIG. 6. Case 3. Photograph of left kidney and ureter showing new growth



A B

FIG. 7. Case 3. *A*, Low power photomicrograph showing papillary nature of intraureteral tumor. *B*, High power photomicrograph of tumor shown in *A*, demonstrating large vesicular nuclei and mitotic figures. A blood vessel appears at upper right. Diagnosis Papillary carcinoma with squamous metaplasia.

urinary bladder the ureter was dilated to about $1\frac{1}{2}$ cm. in diameter and a firm tumor mass could be palpated at this point through the ureteral wall. The ureter was removed in its entirety, including a small cuff of the wall of the bladder surrounding the ureterovesical junction.

The pathologic report was: "The specimen consists of a kidney and entire ureter. Three centimeters from the lower end of the ureter there is a pedunculated fungating mass, with a similar mass just below it measuring 0.3 cm. in diameter (fig. 6). Section through the fungating mass shows it to be composed of broad papillae (fig. 7, *A*) with a thin connective tissue core lined by broad sheets of large cells with large vesicular nuclei (fig. 7, *B*). There are atypical staining and occasional mitotic figures. Sections show the tumor formation to be confined solely to the mucosa and not to penetrate it. Section of the small mass shows it to be composed of a redundant mass of mucosa. Sections of the kidney show some slight arteriosclerotic changes and a few small areas of abscess formation. Diagnosis: Papillary carcinoma of the ureter with squamous metaplasia, early sclerotic changes in the kidney and abscess of the kidney."

The postoperative course was uneventful and there has been no evidence of recurrence up to the present time.

406 St. James Bldg., Jacksonville 2, Fla.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

THE ROLE OF URETERO-INTESTINAL ANASTOMOSIS IN GYNECOLOGY AND FEMALE UROLOGY[1]

LAWRENCE R. WHARTON

Until fairly recently, uretero-intestinal anastomosis was performed quite rarely. This was because of the unfavorable results and high mortality that attended this operation. In recent years, this situation has changed, largely because of chemotherapy, simplification and improvement in the technique of the operation. At the present time, using the simpler techniques, the actual operative mortality of the procedure has almost been eliminated. For example, in 1948, Lanman (personal communication) reported that in the Children's Hospital in Boston, they had performed ureteral implantation on 50 patients without death. It should be stated that these cases were carefully selected beforehand, and practically all were children with exstrophy of the bladder. Almost invariably, only one ureter was implanted at a time and ample time was allowed between implantations to permit adequate recovery. The absence of malignancy eliminated the need for urgency. This series, as well as others, proves that the operation itself, when performed accurately and simply, under favorable conditions, should carry a low mortality.

In other groups, however, especially older persons with malignancy of the bladder or urethra, the situation is entirely different. In such cases, numerous authors have found the operative mortality fully twice as great as in the absence of malignancy (Marshall and Gardner, Hinman and Weyrauch). Also, postoperative complications are greater. Hence, any surgeon whose group of ureteral implantations includes a considerable per cent of malignancies, may expect a higher incidence of complications and a greater mortality.

Even under the most favorable circumstances, however, in the absence of malignancy, and with a normal upper urinary tract, this operation carries a certain degree of unpredictability, as far as the resultant function of the kidneys is concerned. Using a uniform technique, we get a perfect anatomical result in one case, whereas in the next it is followed by a marked hydronephrosis, at times even by complete ureteral occlusion for a few days. At times, this hydronephrosis may persist and result in a functionless kidney which may later require removal. There is hardly an operator who has performed many ureteral implantations, who has not been compelled to do one or more pyelotomies to relieve anuria that occasionally follows operative ureteral edema. Almost invariably, this edema subsides in 5 or 6 days, the ureters begin to drain normally into the sigmoid, and the pyelotomy closes spontaneously. Nevertheless, during these anxious days of uncertainty, most surgeons "play safe" by doing a pyelotomy.

In other words, it is difficult to recall a surgical procedure which is so simple in its performance but which may be followed by so many serious complications. This is probably because of the profound rearrangement of the anatomy and physiology of the upper urinary tract and the employment of a urinary reservoir which is always infected.

---

[1] Read at annual meeting, Mid-Atlantic Section, American Urological Association, Hot Springs, Va., March 11, 1948.

The realization of these facts naturally makes one cautious in recommending the use of uretero-intestinal anastomosis, or in formulating its indications. In the experience of the author and others, however, the incidence of serious complications can be kept low by careful selection of operative cases, adequate preoperative and postoperative care, meticulous attention to operative details, and the use of a simple technique; for as Quinby said in discussing the paper of Hinman and Weyrauch in 1936, "all successful surgery—is simple surgery."

With these facts and limitations in mind, therefore, the author presents a group of cases in which uretero-intestinal anastomosis has been definitely worth while.

GROUP I. EXSTROPHY OF THE BLADDER

We shall discuss this indication very briefly. The first ureterosigmoid anastomosis was performed in 1878 by Thomas Smith in St. Bartholomew's Hospital in London in an unsuccessful attempt to cure exstrophy of the bladder. The patient, a 7 year old boy, died soon after the operation. At the present time, the results in exstrophy are so excellent that it has become one of the standard indications for the operation.

Lanman states that he prefers to perform the operation in children between the ages of 2 and 4 years, although at times, he is compelled to perform it in adults. As the patient with untreated exstrophy gets older, the upper urinary tract usually suffers increasing damage from ureteral obstruction, hydroureter, hydronephrosis, and infection; this is the common cause of death in untreated exstrophy of the bladder.

As a rule, in exstrophy of the bladder, the results of ureteral implantation are excellent, especially when it is done early in life, before irreparable urinary damage has developed. This is shown by Stevens, who collected from the literature the reports of 11 patients who lived longer than 20 years, and one who lived 43 years after the operation. In comparison with the misery of their existence before operation, these persons are naturally grateful.

GROUP II. VESICOVAGINAL AND URETHROVAGINAL FISTULAS, FOLLOWING CHILDBIRTH

Such fistulas are almost always difficult to close. At times, the damage is so great that closure is impossible. Furthermore, even if the fistula is eventually closed, continence is not obtained unless the function of the vesical sphincter can be restored.

Before the development of ureterosigmoid anastomosis, such cases were dismissed as hopeless. Now, however, continence can be restored without undue risk by this procedure.

The following case illustrates the use of ureterosigmoid anastomosis in incurable vesicovaginal fistula. An attractive young woman first came to Baltimore in 1929, at the age of 28 years, as the patient of Dr. Hugh Young. She had been delivered of her first child in Georgia, 3 years previously. The child weighed 14 pounds, and died during delivery. Also the mother suffered a fractured pelvis and a urethrovesicovaginal fistula. She was operated upon by Dr. Young in 1929, and by Dr. Young and myself in 1931, without success. Following these failures, we heard nothing from her for 10 years, until 1941, when she returned. The fistula still occupied most of the base of the bladder and the posterior third of the urethra. The anterior urethra was completely occluded by scar tissue. At that time, I suggested to Dr. Young that we implant the ureters into the sigmoid, and he consented. This operation was therefore done by me in 2 stages, in May and in November 1941. An interesting operative problem arose in this case, in that the right ureter was double down to the bladder wall, having a single opening in the bladder. Fortunately, the 2 ureters were adherent in the pelvic area, and hence they could be treated as one.

The result of these implantations was almost perfect. Repeated functional tests showed that the kidneys were almost normal. On November 24, 1941, eighteen days after the transplantation of the last ureter, the phenolsulphonphthalein test showed an excretion of 30 per cent in the first hour, and 45 per cent in the second hour, a total 2-hour excretion of 75 per cent from both kidneys. The specimens were collected from the rectum. The nonprotein nitrogen of the blood was 30.9 mg. per cent.

Postoperative intravenous urograms showed the result anatomically (fig. 1). On October 31, 1941, five months after the implantation of the right ureters, and about 1 week before the transplantation of the left ureter, the accompanying picture was taken. This shows a normal right urinary tract, excluding the renal and ureteral duplication. In other urograms in this series, the 2 right ureters can be traced to the sigmoid. There is no trace of ureteral dilatation.

After the second operation, there was a moderate dilatation of the left ureter and kidney pelvis. This disappeared, however, and in May 1943, Drs. Waters and Firor reported that the urinary tract was "beautifully visualized and was normal." At about this time, in one of her letters, the patient said she was sorry that she "didn't have this done years ago."

A letter from her family doctor in Georgia, dated February 17, 1948, states that she had married again, had conceived, and carried her pregnancy to the third month when it ended in an abortion. The family doctor said she was in excellent health. Efforts to obtain pyelograms this year have so far been unsuccessful.

GROUP III. URINARY FISTULA, FOLLOWING IRRADIATION

Post-radium fistulas are particularly difficult to close, because of the brawny induration and fixation of the tissues around the fistula. Also, the fear of residual carcinoma in the uterus is constantly present. Such a problem was presented by Mrs. E. F. N., aged 63, who had been given a fairly heavy course of pelvic irradiation, using radium and x-ray, in 1945. Soon after this, she developed complete urinary incontinence due to a fistula which included the right half of the base of the bladder, extended up along the right ureter, into the cervix and thence to the vagina. In other words, it was a vesicocervicovaginal fistula. There was also infection and ulceration of the bladder, with encrustation of urinary salts. In addition, although biopsies from the cervix and fistula showed no carcinoma we could never be quite certain that the deeper tissues did not harbor residual malignant cells For these and other reasons, it seemed futile to try to close the fistula, and ureteral implantation was agreed to

This was done in 2 stages, first, the right side, then the left Several months were allowed to lapse between these 2 implantations because of the frailty of the patient, and because of a chronic respiratory infection

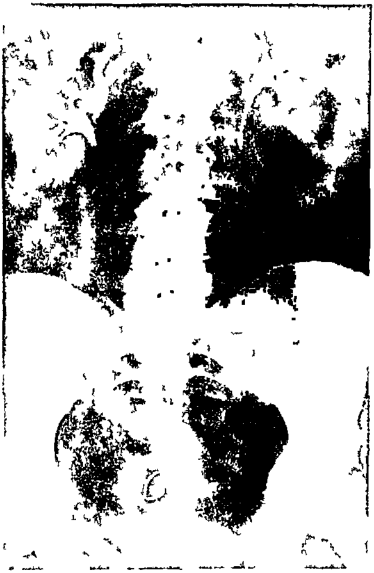


FIG 1 Postoperative intravenous urogram, 5 months after implantation of double right ureters into sigmoid Other urograms at this time show lower ureters to be perfectly normal Left ureter was transplanted a few days after this urogram was taken

Figure 2 is an intravenous urogram that shows the urinary tract 6 months after the implantation of the right ureter, and 3 weeks after implantation of the left ureter into the sigmoid It shows that the right urinary tract is completely normal, having recovered completely from the preliminary slight hydronephrosis There is a moderate hydronephrosis on the left side The patient is now perfectly continent, rarely gets up at night to empty the rectum and is well-satisfied with the management of her problem

GROUP IV AS A PALLIATIVE PROCEDURE IN INOPERABLE CARCINOMA OF THE BLADDER OR URETHRA

In cases of operable carcinoma of the bladder or urethra, in which cystectomy and urethrectomy are anticipated, diversion of the urinary stream is a necessary preliminary step I wish to call attention to the fact that, in certain cases of inoperable carcinoma of the bladder and urethra, implantation of the ureters is a palliative procedure of considerable merit. In these conditions, there are usually distressing vesical symptoms that cannot be relieved by any means. All urologists know too well the agony that such persons suffer.

Recently, the author has had the opportunity to compare the course of such patients with and without ureterosigmoid anastomosis. The contrast is clearly illustrated by the following case.

The patient, a woman 48 years old, noted a little vaginal bleeding for a day or two in August 1947. There was no further symptom of any sort until October 14, 1947, when she suddenly developed complete urinary retention. She was then found to have an inoperable carcinoma of the urethra. The growth was so massive that it almost occluded the vagina. It extended anteriorly to the clitoris, was adherent to the pubic arch, and there were metastases in the inguinal glands. Despite all this, the patient looked perfectly well.

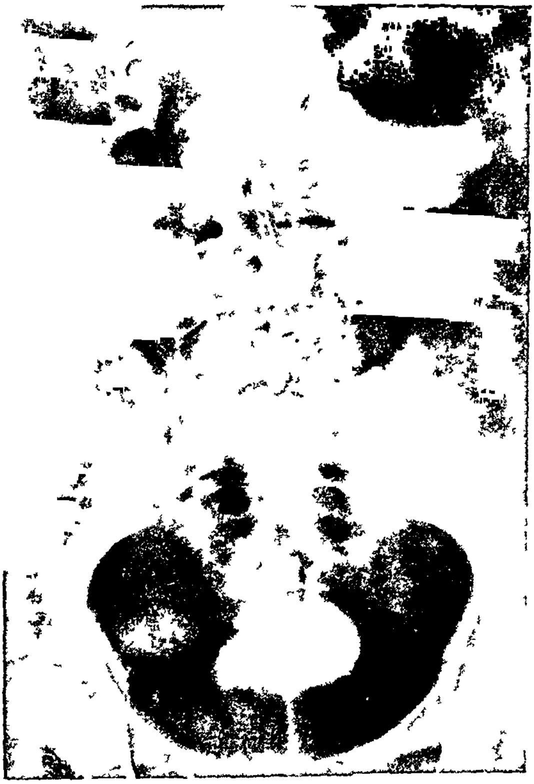


FIG. 2 Intravenous urogram, taken 6 months after implantation of right ureter and 3 weeks after implantation of left. Right urinary tract is completely normal; there is a moderate hydronephrosis of left side.

My aims in this case were two-fold: to make the patient as comfortable as possible and to give her the full benefit of irradiation. The first step was the implantation of both ureters into the sigmoid.

The ureteral implantation was done without any difficulty. Following this, there was a complete anuria for 5 days, during which time the blood nonprotein nitrogen rose to 77 mg. per cent. I therefore did an unilateral pyelotomy, which completely relieved the uremia, and was followed in 2 days by the normal flow of urine from the ureters into the sigmoid. Within a few days the pyelotomy wound closed spontaneously. The ureteral occlusion had apparently been due to edema. The subsequent course was uneventful.

Following this, maximum irradiation was given, but without any appreciable effect on the urethral lesion. It progressed and the whole vagina and urethra became a necrotic, foul, malignant mass.

In spite of this, however, there has been complete relief from all vesical symptoms. The patient has no urinary discomforts whatever, uses the rectum just as one would use a normal bladder, and to that extent leads the life of a normal woman. Figure 3 shows a moderate hydronephrosis; the nonprotein nitrogen was 37 mg. at this time, 2 months after the implantation of the ureters.

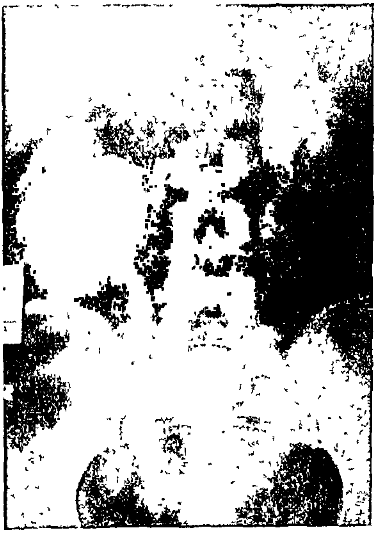


FIG. 3 Intravenous urogram, taken 2 months after implantation of both ureters into sigmoid, for carcinoma of urethra. Rather marked bilateral hydronephrosis and hydroureter.

This is in marked contrast with the condition of other persons who have similar lesions but in whom the urinary stream has not been diverted.

Because of the striking relief afforded in this instance, the author takes occasion to stress the value of this procedure merely as a palliative measure in certain inoperable cancers of the bladder or urethra. It not only completely relieves all symptoms associated with micturition, but permits the use of intense irradiation, excision or local treatment of the bladder or urethra, by completely isolating these organs from the upper urinary tract and depriving them of all function.

The author does not recommend the routine use of ureterosigmoid anastomosis, by any means, in all cases of inoperable carcinoma; but in selected cases, it may grant welcome comfort.

CONCLUSION

Ureterosigmoid anastomosis is a rather simple operation, as far as its technical performance is concerned. But it may be followed by distressing and persisting sequelae, and the occurrence of these complications is unpredictable. They are particularly liable to develop if both ureters are implanted at one time, in adults with malignant conditions in the genito-urinary tract, and in persons with hydronephrosis, hydro-ureter, and urinary infection.

In most cases, according to our experience, there is postoperative hydronephrosis and hydroureter, which often clears up completely, leaving occasionally a perfectly normal urinary tract. At times, however, this dilatation may progress and may lead to destruction of the kidney.

In properly selected cases, however, the operation can be done with relative safety and assurance of a good result.

In spite of risks, there are certain conditions in female urology and gynecology in which the operation is definitely indicated as the only means of correcting permanent urinary incontinence and obtaining symptomatic relief from an inoperable malignancy. In such cases, the palliative value of ureterosigmoid anastomosis is worth consideration.

1201 N. Calvert St., Baltimore 2, Md.

REFERENCES

Boeckel, A.: De L'Exclusion De La Vessie Dans La Tuberculose Réno-Vésicale. J. d'urol. **I**: 345–372, 1912.

Hinman, F. and Weyrauch, H. M.: A critical study of the different principles of surgery which have been used in uretero-intestinal implantation. Trans. Am. Assn. Genito-Urin. Surg., **39**: 15–178, 1936.

Ladd, W. E. and Lanman, T. H.: Exstrophy of the bladder and epispadias. New Eng. J. Med., **222**: 130–134, 1940.

Marshall, V. F. and Gardner, J. S.: An evaluation of the Coffey I method for uretero-intestinal anastomosis. Surg., Gynec. and Obst., **81**: 559–574, 1945.

Smith, T.: An account of an unsuccessful attempt to treat extroversion of the bladder by a new operation. St. Barth. Hosp. Reports, **15**: 29–35, 1879.

Stevens, A. R.: Longevity following uretero-intestinal anastomosis. J. Urol., **46**: 57–66, 1941.

Wharton, L. R.: Uretero-intestinal anastomosis. Implantation of double ureter. End result. J. Urol., **48**: 474–488, 1942.

Wharton, L. R.: Ureteral implantation and chemotherapy. Section XXI in Gynecology Including Female Urology. Philadelphia: W. B. Saunders Co., 1947, 2nd ed., pp. 956–991.

The Journal of Urology
Vol. 61, No. 1, January 1949
Printed in U.S.A.

VESICO-APPENDICEAL FISTULA[1]

HERMAN J. MEISEL, HAROLD N. KAGAN AND JOSEPH M. MILLER

The creation of a vesico-intestinal fistula by a process primary either in the intestine or the bladder is a serious complication which confronts the urologist and the surgeon but infrequently. The prognosis is poor so that the choice of treatment must be guided by great care. One type of vesico-intestinal fistula forms the exception in this group, for the results of simple surgery are excellent. These are fistulas of the appendix, but unfortunately they form but a small portion of the entire group. In a total of 592 vesico-intestinal fistulas of all types Kellogg offered the following statistics for the more frequently appearing types of fistulas: fistulas of the sigmoid, 63 per cent; fistulas of the rectum, 16 per cent; fistulas of the ileum, 4 per cent; and fistulas of the appendix, 4 per cent. The appendix was involved in 27 cases in this group. Higgins reported a group of 382 such cases of which 13 were of appendicular origin. Observations concerning 5 patients with vesico-appendiceal fistula, with one in detail, have been reported by Pemberton, Poole and one of us (J. M. M.).

When the cecum is in the normal anatomic position, an extremely long appendix, which is the seat of an acute inflammation must be present to result in adherence or close approximation to the bladder. A mobile cecum with an inflammed appendix of average length may also cause either result.

Many of these patients with vesico-appendiceal fistula give a history of acute appendicitis. Some patients will completely deny symptoms of a previously existent acute inflammatory process of the appendix.

The symptoms of vesico-intestinal fistula are essentially the same whatever the cause may be. A history of lower abdominal distress is usually obtained. Burning and frequency of urination occur. Micturition may occur hourly, and may be accompanied by pain or terminal hematuria. Chills and elevation of temperature may occur. Bubbles of gas may be passed through the urethra, usually at the end of urination. The passage of feces in the urine will not be noted as often. The fecal content of the urine will be conditioned by the state of the bowels. With a constipated state, none or little fecal material will be seen in the urine. The onset of liquid stools may increase the quantity of fecal material in the urine. When the flow is such a fistula is reversed, and the urine is diverted into the bowel, slight laxity of the bowels or a chronic diarrhea may result.

The presenting symptoms may be those of urinary disturbance alone. Careful and repeated examinations are necessary to discover the true causative factor in the intestine.

Cystoscopy is necessary and invaluable in the diagnosis. The discovery of calculi in the bladder in vesico-intestinal fistula is rare. In vesico-appendiceal fistulas the orifice is usually present on the right of the bladder. An aperture may not be seen for a mass of granulation tissue or a depressed necrotic region in the bladder may be the only evidence seen through the cystoscope that a fistula exists. Occasionally gas and less often feces may be seen passing through the orifice of the fistula. When suspicion of a fistulous tract is present, a ureteral or a lead catheter may be passed very gently through the aperture and a substance opaque to the roentgen rays may be injected. The fistulous tract and part of the colon may be outlined. Force in passing the catheter must be avoided as the creation of a false passage is a definite hazard. Cystograms may be of value as the medium may outline the abnormal tract. Methylene blue may be instilled into the bladder or rectum and recovered from the opposite location to prove that a fistula is present. Similarly, charcoal may be administered orally and recovered in the urine. Roentgenographic examination of the colon may reveal a tract passing to the bladder. Barium may be passed in the urine after such an examination.

---

[1] Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

The treatment of the vesico-appendiceal fistula is comparatively simple in contrast to the other types of vesico-intestinal fistula. Cultures of the urine should be made and the appropriate chemotherapy or antibiotic administered. Enough fluid should be given to insure a urinary output of 1200 cc in 24 hours. Freeing the appendix from the bladder, closure of the aperture in the latter and the removal of the appendix comprise the surgical treatment. An indwelling urethral catheter should be kept in place for about 10 days. Such treatment promises an excellent result with a low mortality.

Illustrative of patients who have vesico-appendiceal fistula is a 25 year old white man who stated upon admission to the hospital that he had had intermittent sharp pain in the lower abdomen accompanied by 2 to 4 diarrheal stools a day for about 3 weeks. Frequency, terminal hematuria, and some straining upon urination had been present for about 2 weeks. The patient stated that he passed gas with his urine for about 1 week.

A history of a previous similar episode was not obtained. The patient stated that he had had an episode of lower abdominal pain for which he was admitted to a hospital about 4 years ago. Detailed questioning did not reveal symptoms suggestive of acute appendicitis at any time.

Physical examination was not very revealing. A slight degree of tenderness was present over the lower abdominal region, particularly over the midsuprapubic area. Upon rectal examination the left seminal vesicle was found to be firm, enlarged, but not tender.

Studies of the components of the peripheral blood revealed them to be essentially within normal limits. The urine was found to be alkaline and to contain albumin, graded 1 on a scale of 4, numerous erythrocytes and 10 leucocytes per high power field. Culture of the urine disclosed Proteus vulgaris and microaerophilic gamma streptococcus. A subsequent culture of the urine from the bladder revealed that Proteus vulgaris and Escherichia coli were present.

A survey film of the abdomen revealed a dense shadow of calcification measuring about 4 by 2½ cm. overlying the area of the bladder. Cystoscopy was done and the mucosa of the bladder was found acutely inflammed. A large soft calculus, which was easily movable, was found in the region of the trigone. A small area of ulceration was seen in the right side of the fundus. It was possible to pass a ureteral catheter for only about 1 cm. into the ulcerated area. The cystogram done with 200 cc of 6 per cent skiodan showed a smoothly contoured bladder with the escape of radiopaque material into the cecum. Excretory urography was done and the upper urinary tract was found to be normal.

Roentgenographic examination of the colon did not demonstrate the fistula. Barium, however, was passed with the urine in the period subsequent to the examination, thus confirming the presence of a fistula.

The patient was given enemas and sulfasuxidine in preparation for operation. A Foley catheter was inserted into the bladder on the day of operation, since intraperitoneal exposure and excision of the fistula were planned.

At operation a very mobile cecum with a moderately long appendix attached to the bladder was found. An easily demonstrable fistula was present between an area at about the junction of the proximal two-thirds and the distal one third of the appendix and the right portion of the dome of the bladder. Gross evidence of inflammation was lacking. A small cuff of bladder was removed from around the site of the fistula and the calculus was extracted from the bladder. Closure of the bladder by inversion, appendectomy and closure of the abdomen was then accomplished.

The postoperative course was without incident. The administration of sulfadiazine and penicillin was continued for 5 days and the Foley catheter was left in place for 7 days. The patient was discharged on the thirteenth postoperative day asymptomatic and with clear urine.

Pathologic examination revealed chronic inflammatory changes throughout the appendiceal coats. Chemical analysis of the calculus revealed it to be composed of carbonates, phosphates and proteins.

SUMMARY

A case of vesico-appendiceal fistula has been presented which illustrates the preciseness with which a diagnosis can be made provided there is a high index of suspicion directed towards the symptom of pneumaturia. The appearance of even one or two bubbles of gas in the urine, even though on rare and widely separated occasions, calls for thorough investigation of the possibility of vesicoenteric fistula by the methods described previously. Fortunately cystoscopic investigation is usually indicated at once and this often simplifies the problem by revealing a suggestive lesion or an actual fistulous opening. In the case of vesico-appendiceal fistulae, the brilliance and permanence of the results of a simple operative procedure amply reward every effort put into the diagnostic search.

REFERENCES

Higgins, C. C.: Vesico-intestinal fistula. J. Urol., 36: 694–709, 1936.
Kellogg, W. A.: Vesico-intestinal fistula. Am. J. Surg., 41: 135–186, 1938.
Pemberton, J. de J., Pool, F. L. and Miller, J. M.: Vesico-appendiceal fistulas. J. Urol., 44: 274–278, 1940.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

EXPERIENCES WITH RETROPUBIC PROSTATECTOMY[1]

THOMAS D. MOORE

From the Department of Urology, John Gaston Hospital, College of Medicine, University of Tennessee, and the Moore Clinic, Baptist Memorial Hospital, Memphis, Tennessee

An historical review of the retropubic approach for the purpose of prostatectomy has been recorded by Millin, and more recently by Bacon and Lowsley.

In a discussion of the advantages of the retropubic approach as compared to the three other standard procedures, namely perineal, suprapubic and transurethral, numerous features require consideration with special reference to the size of the gland, the type of obstruction, the habitus of the patient and his status as a surgical risk. There are good reasons why any one of the four procedures may be used in a selected case as the operation of choice but in weighing the advantages on a comparative basis the surgeon would naturally choose for the majority of cases the procedures which in his hands have produced the most satisfactory functional results with the least risk and with the shortest and smoothest convalescence. After hearing Millin's presentation of the subject, I decided to try the operation in a series of cases and to compare the results with two similar consecutive series of cases, comparable in their clinical features, which had been subjected respectively to primary suprapubic prostatectomy and transurethral prostatic resection. The comparison might be more complete were a similar series of perineal prostatectomies included but I am frank to admit that I am not a perineal prostatectomist.

In spite of the dictum "Be not the first to try the new nor the last to lay the old aside" it has been my privilege to perform 46 retropubic extravesical prostatectomies, 43 primary and 3 secondary, on my private patients and on my service at the University of Tennessee during the past 7 months. Some years ago after performing transurethral resections almost routinely on nearly all patients suffering from prostatic obstruction the conclusion was reached that in the very large glands enucleation through an incision was a wiser procedure incurring less loss of blood, less risk, a shorter convalescence and a more satisfactory functional result. The choice of suitable cases for retropubic prostatectomy was therefore made mainly on the basis of the large size of the glands which were considered unsuitable for transurethral prostatectomy. In the recent past these cases would have been subjected to primary suprapubic prostatectomy. It might be of interest to state that during the period of 7 months in which this series of 46 retropubic prostatectomies were performed in my private practice and on the University service 2 primary suprapubic prostatectomies and 193 transurethral prostatic resections have been carried out. All of the retropubic operations included in this discussion have been for benign obstructions although it has been my privilege to date to encounter early carcinomas of the prostate in 2 cases in which a radical retropubic prostatectomy was performed.

---

[1] Read at annual meeting, Mid-Atlantic Section, American Urological Association, Hot Springs, Va., March 12, 1948.

After this brief experience with the retropubic approach the impression has been gained that this operation has definite advantages as compared to primary suprapubic prostatectomy. Noteworthy are the greater degree of comfort, less evidence of shock, the omission of suprapubic vesical drainage and the smoother and shorter convalescence, all of which are distinct advantages which have been attained without subjecting the patient to an increased hazard.

For somewhat similar reasons the retropubic approach appears more desirable than the transurethral in patients with large glands in that the operation is not as time-consuming nor as difficult and the average patient requires less of the surgeon's time and attention in the postoperative period. The advantages from the standpoint of the patient also appear definite in that the operation is concluded at one sitting, there is less bleeding postoperatively, the period of convalescence is about equal, the risk is no greater, there is less discomfort in the immediate postoperative period and the functional results in the main are superior.

EXAMINATION AND PREPARATION OF THE PATIENT

Presented with a patient suffering from prostatic obstruction his examination includes a general physical survey, routine urinalysis of a 2 glass specimen if he is able to micturate, a test for residual urine employing a rubber catheter of small caliber, and a pneumocystogram with the patient in the semi-lateral position. The functional state of the kidneys is determined by an estimation of the nonprotein nitrogen in the blood and later by the phenolsulphonphthalein output for 2 hours divided into 30 minute periods. In some cases where it seems advisable, but not routinely, an excretory urogram is obtained. The combination of the digital examination of the prostate and the shadow of the gland as visualized in the pneumocystogram afford a fairly reliable estimate of the type of obstruction and the size of the gland. It has not been our custom to subject these elderly patients to cystoscopic examination unless there is some special indication for the instrumentation. Routine inspection of the bladder is reserved for those cases to be resected transurethrally, when cystoscopy is employed under anesthesia immediately preceding the operation. Millin advocates cystoscopy under anesthesia for a decision at the time of operation as to the choice between the retropubic or transurethral approach and then proceeds with either. In our experience cystography in most cases permits this decision and the operation of choice can thus be scheduled in advance.

Preliminary treatment includes the judicious use of the sulfonamides, in many cases as a prophylactic and *in others for the control of an active urinary infection.* If residual urine amounts to 60 cc or more a 16 F. Foley catheter is left in for continuous drainage. The patient is observed daily in the hospital and he receives appropriate attention to his cardiovascular system. A large fluid intake is maintained and as soon as his general condition seems favorable and tests for renal function appear satisfactory the operation is scheduled. Vas ligation or partial vasectomy is deferred until the time of the operation.

OPERATIVE TECHNIQUE FOR RETROPUBIC PROSTATECTOMY

Special instruments designed by Millin have only recently become available and definitely facilitate the operative procedure. During the period in which these instruments were unobtainable a Balfour retractor was substituted for Millin's special retractor with the aid of a spatula for depressing and traction of the bladder upward. Babcock's forceps with long handles were substituted satisfactorily for the special T capsule forceps and a long needle holder had served very well in place of the special long boomerang needle.

Either the standard suprapubic midline incision or a transverse incision about 2 cm. above the symphysis may be employed. We have preferred the latter, in which the anterior sheath of the recti muscles is incised. The muscles are separated from the sheath several centimeters above and below by finger dissection, followed by separation with scissors of the linea alba from the sheath, permitting wide retraction of the recti muscles which do not require division as is practiced by some surgeons. With the patient in the Trendelenburg position easy access to the retropubic space is permitted. The anterior aspect of the prostate gland is separated by gauze dissection from the symphysis pubis, when there may be seen one or more veins receiving blood from the dorsal vein of the penis and other tributaries coursing upward and laterally on approaching the region of the vesical neck. Hemostatic ligatures may be passed beneath the veins deeply behind the pubis but we have found it more satisfactory to secure them with hemostats and electrocoagulation. Mobilization of the prostate anteriorly and laterally is carried out with sponge sticks and the lateral spaces lightly packed with gauze strips, thus stabilizing the gland and removing from the field fatty tissue which might otherwise interfere somewhat with good visualization of the prostatic capsule. A short transverse incision is then made in the capsule well below its juncture with the vesical neck. This may be accomplished with a scalpel or preferably in our experience with a needle electrode and cutting current. The use of electrosurgery in this connection has not appeared to interfere with primary healing. An open end aspirator follows closely the incision as bleeding from the incised capsule may be profuse. On reaching the whitish adenomatous tissue the capsule is separated laterally and anteriorly with curved forceps or flat scissors entered in the cleavage plane. The margins of the incision are grasped with the special T capsule forceps which serve very well for hemostasis and upward traction. A finger is then introduced into the cleavage plane and working laterally and downward the adenomatous lateral lobes are separated from the deeper portions of the capsule. Finally the urethra is severed near the apex with scissors and the lobes are reflected upward and brought out of the incised capsule with the assistance of vulsellum forceps. In this maneuver the prostatic capsule may require incising more widely in large adenomas. Upward traction with vulsellum forceps assists greatly and in most cases has rendered unnecessary elevation of the gland digitally from the rectal side. The partially delivered adenomatous mass remains attached at the inferior margin of the vesical neck. If a subcervical or subtrigonal adenoma co-exists it is enucleated from below upward and finally the attachment is clamped with curved forceps, divided with scissors and the stumps electrocoagulated for hemostasis. A gauze strip is packed into the capsule temporarily and at this point if a ledge of tissue seems to persist at the inferior margin of the vesical neck it is corrected by excising a V-shaped wedge, the margins of which are also electrocoagulated. The gauze pack is then removed from the capsule and a small selfretaining spring-wire retractor, such as is commonly used in thyroidectomy, is inserted in the capsule permitting visualization of its interior. Any remaining tags of prostatic tissue or small adenomas are removed secondarily and all bleeding points are visualized and controlled. It has been our custom to introduce a finger through the vesical neck into the bladder and palpate for possible calculi, diverticular orifices or neoplasms. Stones if present may be grasped and removed through the vesical neck if not too large, and large diverticula may be removed extravesically as occurred in one instance in this series. Large calculi may require incising the vesical neck in the midline to permit their removal, in much the same way that an episiotomy is performed. A 24 F. Foley catheter is then passed per urethram, the tip of which is drawn through the incision in the prostatic capsule. A single layer of oxidized gauze, saturated with a suspension of colloidal sulfathiazole, is perforated in its center and the tip of the catheter and bag are drawn through the opening in the gauze. The bag is then partially distended with 15 to 30 cc of fluid and drawn into the prostatic cavity, carrying with it the oxidized gauze. The latter is tucked about the bag and the tip of the catheter is then directed through the vesical neck into the bladder. In many cases where the prostatic capsule shows very little evidence of oozing the use of oxidized gauze is omitted. The prostatic capsule is then closed with an inner row of chromic O catgut interlocked and an outer row of the same suture material, thus effecting a water-tight closure. One Penrose drain is left in the retropubic space. The recti muscles are approximated loosely with one or two interrupted sutures of plain catgut and the sheath of the recti is closed with interrupted cotton No. 30. This suture material is also employed in closing the skin. Bilateral subcutaneous ligation of the vasa is carried out as a prophylactic against epididymitis before the patient leaves the operating room and 30 cc of a solution of neutral acriflavine containing sodium citrate 1 per cent is injected through the catheter and left in the bladder for the prevention of clots pending the return of the patient to his hospital bed, where a closed system of drainage and irrigator containing the same solution is connected. The oozing of blood in the immediate postoperative period is of a negligible degree in most cases and within a few hours the urine may be barely pink. This tendency to ooze has been strikingly less in the retropubic cases than with either suprapubic prostatectomy or transurethral resections.

SUPRAPUBIC, RETROPUBIC AND TRANSURETHRAL PROSTATECTOMY: COMPARATIVE DATA

An attempt has been made to portray a fair comparison in the three series of cases. In those in which the suprapubic and retropubic approaches were employed consecutive cases have been reviewed and their clinical investigation, preoperative treatment and postoperative care have been along similar lines and urethral series catheter drainage was maintained from 2 to 22 days, averaging 6 (table I). Thus it may be seen that the average period of urethral catheter drainage was the same in the retropubic and transurethral series but that this postoperative period of drainage averaged 6 days longer in the suprapubic cases. This may be explained by the more prompt healing of the immobile prostatic capsule, whereas in suprapubic prostatectomy the wall of the bladder, a distensible organ, does not lend itself so readily to a prompt and secure healing.

Postoperative temperature. The maximum postoperative temperature and duration of fever might serve as an index to the degree of a satisfactory convalescence. In the suprapubic series the maximum temperature varied from 99.2 to 104 F, averaging 101.5 F. In the retropubic series the maximum postoperative temperature varied from 99.4 to 105.4 F, averaging 102 F. In the transurethral series the maximum postoperative temperature varied from 99 to 105.6 F, averaging 101.5 F. The higher temperatures attended such complications as septicemia, acute pyelonephritis and acute epididymitis. A temperature of 99 F or more was regarded as fever, some degree of which persisted from 2 to 42 days in the suprapubic series, averaging 8½ days; from 2 to 17 days in the retropubic series, averaging 7 days; and from 1 to 23 days, averaging 5, in the transurethral series (table 1). It would seem from this comparison that there was very little difference in the average maximum temperatures in the three series although the febrile course was of somewhat shorter duration in the retropubic series than in the suprapubic group. It was of still shorter duration by two days on the average in the transurethral series.

TABLE 1. *Comparative postoperative data on primary suprapubic, retropubic and transurethral prostatectomy; 46 cases in each series*

		Average	
Maximum postoperative temperature	99.2° to 104°	101.5°	Suprapubic
	99.4° to 105.4°	102.0°	Retropubic
	99° to 105.6°	101.5°	Transurethral
Duration of fever	2 to 42 days	8½	Suprapubic
	2 to 17 days	7	Retropubic
	1 to 23 days	5	Transurethral
(Fever: 99° or more.)			
Catheter removed	7 to 27 days	12	Suprapubic
	3 to 18 days	6	Retropubic
	2 to 22 days	6	Transurethral
Postoperative hospitalization	10 to 43 days	15	Suprapubic
	6 to 19 days	11	Retropubic
	5 to 26 days	11	Transurethral

Incisional healing. The routine use of chemotherapy and the antibiotics, both before and after the operation, undoubtedly has been a contributing factor in healing per primam of the incision, which was attained in 42 of the suprapubic series and in 34 of the retropubic cases. Pseudomonas aeruginosa was the predominant organism in 2 of the 12 patients subjected to retropubic prostatectomy who developed evidence of infection in the wound in spite of sulfonamide and penicillin therapy. There was moderate elevation of temperature and the incisions developed evidence of suppuration, which very promptly subsided on the administration of streptomycin. In the other 10 cases the degree of infection was mild and in all fairly prompt and complete healing occurred.

Blood transfusions. Blood transfusions in the postoperative period were given to 8 in the suprapubic series, to 12 in the retropubic series and to 15 in the transurethral series. Often transfusions were not urgently necessary but were considered advantageous on the basis of replacement of blood lost or to combat shock, most often of a mild degree.

Period of postoperative hospitalization. The period of postoperative confinement in the hospital in the suprapubic series varied from 10 to 43 days, averaging 15 days. In the retropubic series the period of postoperative confinement varied from 6 to 19 days, averaging 11. None of the patients were discharged from the hospital until the incision was dry with one exception. A diabetic patient had no desire to live and made no real effort to regain bladder function; in spite of a suprapubic prostatectomy and the subsequent transurethral removal of a small amount of tissue he made no effort to micturate and was permitted to leave the hospital with a small suprapubic tube in place. His postoperative period of confinement in the hospital was 43 days. After his return home it was reported that his bladder function was satisfactory. In the transurethral series the period of postoperative hospitalization ranged from 5 to 26 days, averaging 11. Therefore, the vaunted short stay in the hospital so long proclaimed as an advantage for the transurethral approach was equaled in this series by those enucleated retropubically, the average period of both series being 11 days (table 1).

Thus it may be seen that the postoperative course in retropubic prostatectomy compares favorably with that of transurethral resection and is more favorable than in the suprapubic series. We have been impressed by the greater comfort experienced by the patient subjected to retropubic prostatectomy as compared with the suprapubic and transurethral cases and in the first 24 to 48 hours of the postoperative period there has been less evidence of shock.

Immediate functional results. In the series treated suprapubically the immediate functional results were satisfactory in 44. In 1 case the incision remained dry for 48 hours after removal of the urethral catheter and the patient was discharged on the tenth postoperative day. He was re-admitted to the hospital six days later because of the re-opening of the suprapubic sinus with profuse leakage of urine. On re-insertion of a urethral catheter the sinus closed and he was allowed to return home 3 days later. In another case previously referred to, the patient was allowed to return home with a small suprapubic tube in place on the forty-third postoperative day. Prior to his dismissal inspection of the vesical neck employing a resectoscope revealed no definite obstructive factor but 4 gm. of additional tissue was removed, in spite of which difficulty persisted.

The immediate functional results in 44 of the retropubic cases were satisfactory in that the bladder emptied freely, completely and with normal control. In 1 required incision or drainage and bacteriological studies have therefore not been conducted. Treatment has consisted of rest in bed, the application of infra-red heat, intensive courses of streptomycin and penicillin, and daily injections of thiamine hydrochloride. Six of the patients were able to be up and about with fair comfort within a week after beginning treatment and in the other two the response was slower. The disease is said to be self-limited with symptoms usually persisting from 2 to 6 months or longer, according to Lavalle and Hamm.

In my experience osteitis pubis is by far the most disturbing complication incurred in retropubic prostatectomy, warranting a searching investigation as to the etiologic factors and their scrupulous avoidance if possible.

Mortality. In the suprapubic cases there was 1 death from coronary occlusion on the second postoperative day. In the retropubic series there was no immediate mortality in the hospital, all of the patients having been discharged with an average postoperative stay of 11 days. In the transurethral group there were 2 deaths, one from pulmonary embolism on the tenth postoperative day and the other from pneumonia on the twelfth day.

LATE FUNCTIONAL RESULTS FOLLOWING RETROPUBIC PROSTATECTOMY

It has been our privilege to have observed 25 of these cases as late as 4 to 7 months following retropubic prostatectomy. In all of them urinary control was normal. Twenty-three were tested for residual urine and none was found. In 12 cystograms were obtained with the bladder comfortably full and a second film while voiding. In many of these there was evidence of an intact internal vesical sphincter (fig. 1). In a few a small prostatic cavity was visualized (fig. 2). In 17 the urine was clear. In 2 there was grade 1 infection, in 4 there was grade 2 pyuria and in 1 grade 3. In 1 case, in which there was grade 4 infection, the patient was experiencing urinary difficulty because of a urethral meatal stricture, the dilatation of which restored free bladder function. Its effect on the pyuria has not been determined. Four of the 25 cases had developed osteitis pubis from 3 weeks to 5 months postoperatively. Two had fully recovered within 1 month of the onset and 1 within 2 months; the fourth patient had developed this complication 4 months postoperatively and had not fully recovered 1 month later but was able to be up and about.

Considered as a group it may be stated that the late functional results were highly satisfactory in the 25 patients observed from four to seven months postoperatively.

SUMMARY

A comparatively brief experience with 46 consecutive retropubic prostatectomies following fairly closely the technique described by Millin is discussed. In an endeavor to evaluate and compare the procedure with primary suprapubic prostatectomy and transurethral prostatic resection a similar number of consecutive cases treated by these two approaches respectively are also reviewed. The analysis of the data derived from this study indicates that the comparison is fair in that all of the patients were of a similar age group and were suffering from essentially the same degrees of prostatic obstruction and were patients with much the same infirmities Their examinations and preliminary preparation were along the same lines as was also their postoperative care Although the series is small and does not warrant the drawing of conclusions there is definite evidence that retropubic prostatectomy is an operation perhaps more easily mastered than transurethral resection but somewhat more difficult than removal of the prostate suprapubically The impression has been gained from this brief experience that the patients are more comfortable in the immediate postoperative period, healing is prompt, the operation incurs no greater risk and the period of hospitalization is shorter than in those dealt with suprapubically and about equal to those treated transurethrally In my experience the most serious deterrent to the retropubic approach is the fairly frequent occurrence of osteitis pubis

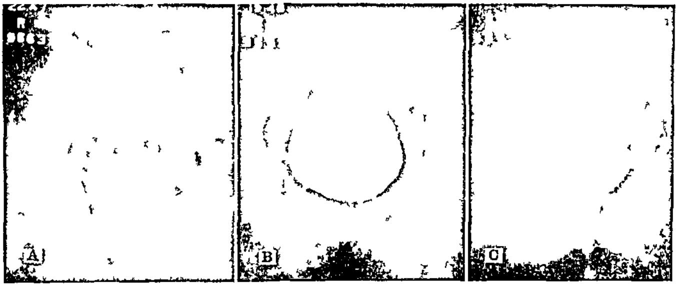


FIG 1 *A*, Preoperative pneumocystogram revealing intravesical posterior commissural prostatic hypertrophy of unusual degree *B*, Cystogram obtained 5 months following retropubic prostatectomy Note evidence of intact internal vesical sphincter *C*, Voiding cysto urethrogram, which reveals small prostatic cavity and absence of evidence of obstruction

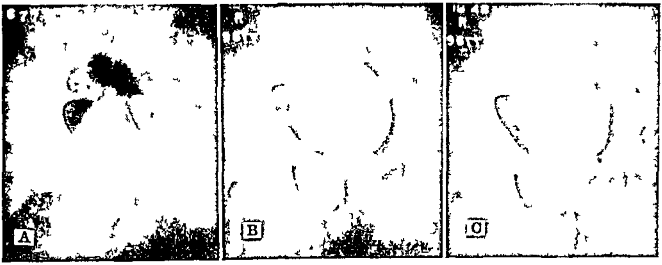


FIG 2 *A*, Preoperative pneumocystogram Note wide intravesical prostatic hypertrophy, largest gland in the retropubic series weighing 250 gm *B*, Cystogram obtained 5 months following retropubic prostatectomy *C*, Voiding cysto urethrogram Note persistence of small prostatic cavity and evidence of normal bladder function

Should the prevention of this distressing complication prove to be possible the operation will probably become a standard surgical procedure in urologic practice and perhaps will replace to a great extent suprapubic prostatectomy for hypertrophies of unusually large degree.

899 Madison Ave., Memphis 3, Tenn.

REFERENCES

BACON, S. K.: Retropubic prostatectomy; an extravesical technique; report of 32 cases. J. Urol., **59**: 376, 1948.

JACOBS, L. C. AND CASPER, E. J.: Pre-vesical prostatectomy. Urol. & Cutan. Rev., **37**: 729–732, 1933.

LAVALLE, L. L. AND HAMM, F. C.: Osteitis pubis: Its diagnosis and treatment. J. Urol., **61**: 83, 1949.

LOWSLEY, O. S. AND GENTILE, A.: Retropubic prostatectomy. J. Urol., **59**: 281, 1948.

MAIER, O.: Arch. klin. Chir., **132**: 296, 1924. (Quoted by Millin.)

MILLIN, T.: Retropubic Urinary Surgery. Edinburgh: E. & S. Livingstone Ltd., 1947.

——: Retropubic prostatectomy. J. Urol., **59**: 267, 1948.

VAN STOCKUM, W. J.: Zbl. Chir., **2**: 41, 1909. (Quoted by Millin.)

THE JOURNAL OF UROLOGY
Vol 61 No 1, January 1949
Printed in U S A

RETROPUBIC PROSTATECTOMY[1]

DAVID PRESMAN AND HARRY C ROLNICK

From the Departments of Urology, Cook County Hospital, Michael Reese Hospital and the Chicago, Medical School, Chicago, Ill

Removal of the obstructing benign prostate by the retropubic route has been recently popularized by Millin of England His results in a large series of cases have been extremely satisfactory and have stimulated a renewed interest in the possibility of further decreasing the mortality and morbidity figures of prostatic surgery The lack of agreement among urologic surgeons as to the preferred operation for removing a hypertrophied prostate gland attests to the fact that each of these techniques has its disadvantages and drawbacks The proponents of transurethral resection, suprapubic transvesical prostatectomy, and perineal prostatectomy are fully aware of certain deficiencies in their respective operation, maintaining, however, that complications and technical difficulties are fewer than in the other procedures In view of this disagreement, further progress in surgery of the prostate gland will best be served by fully investigating the potentialities of any new method which offers improvement in operative results

The evaluation of any technique of prostatectomy may be divided into three aspects, a) the actual operative procedure with its attendant mortality, b) the morbidity and postoperative complications, and c) the functional end results *Our experience with retropubic prostatectomy, although not large, is sufficient* to offer a clinical impression of the operative procedure and the postoperative course The follow-up on our patients has not been long enough to make an unequivocal statement as to the final end results The evaluation of the functional end results awaits the more widespread utilization of this new operation by many urologists and an adequate follow-up study over a longer period of time This report is presented to emphasize the soundness of retropubic prostatectomy as an operative procedure in the hope that a greater experience will be accumulated among urologists so that its true place in prostatic surgery can be decided

From a theoretical viewpoint, the retropubic operation is the most logical approach to the hypertrophied prostate because of two important factors 1) It is the shortest and most direct route, and 2) there are no important organs or structures which can be traumatized during the operative procedure

SURGICAL ANATOMY

From the anatomical viewpoint, the retropubic approach to the prostate is the most direct one and does not involve any important organs or structures that may be a cause of postoperative complications Practically the entire operation is performed within the space of Retzius which is actually only a potential space between the prostate and the pubis The structures in the space of Retzius which must be traversed in order to reach the prostate gland are as follows (fig. 1): 1) loose areolar and fatty tissue; 2) the anterior prostatic plexus of veins; 3) the prostatic fascia; 4) the true and false capsules of the prostate.

---

[1] Read at meeting of Chicago Urological Society, January 22, 1948

The loose areolar and fatty tissue lies between the prostatic urethra with its coverings and the pubis. It is easily separated from these structures by careful blunt dissection with the fingers or a sponge so that the prostatic urethra is fully exposed. It usually contains large branches from the anterior prostatic plexus of veins.

The anterior prostatic plexus of veins (plexus of Santorini, pudendal plexus, vesicoprostatic plexus) is the principal structure that offers any problem to the operator. This plexus is composed of relatively large channels running, for the most part, in a longitudinal direction on the anterior and lateral aspects of the prostatic urethra. The veins are situated within the fibrous sheath or fascia of the prostatic urethra but several large branches ramify throughout the areolar and fatty tisse lying between the prostate and the pubis. The blood supply of the plexus is derived mainly from the deep dorsal vein of the penis and from the prostate gland. The plexus communicates freely with the hemorrhoidal and vesical plexuses and empties eventually into the hypogastric vein.

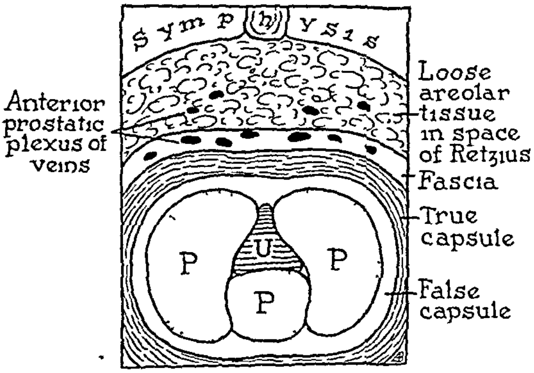

Symphysis
Anterior prostatic plexus of veins
Loose areolar tissue in space of Retzius
Fascia
True capsule
False capsule
P
U
P
P

FIG. 1. Diagrammatic representation of cross-section through prostatic urethra just below vesical neck Size relationship of various structures are distorted for sake of clarity. *P*, Hypertrophied prostate, *U*, lumen of prostatic urethra

The prostatic fascia (endopelvic fascia) is a sheath-like structure which encircles the prostate. Anteriorly, it is thin and is closely adherent to the true capsule of the prostate. It contains the main channels of the anterior prostatic plexus of veins.

The true and false capsules of the prostate do not appear as separate and distinct structures but rather as a single fused layer surrounding the prostate. The thickness of this capsular layer is striking, usually being from 1.0 to 1.5 cm. Its thickness is very apparent when it is incised during retropubic prostatectomy in order to expose the prostate. The capsule is rather vascular but very little bleeding occurs when it is incised if preliminary suture-ligature of the anterior plexus is performed. This will be described later.

OPERATIVE TECHNIQUE

We have followed the fundamental technique of retropubic prostatectomy as described by Millin with, however, several modifications in an attempt to simplify the procedure as much as possible. By means of these modifications, the operation can be performed very expeditiously without the aid of any special instruments or equipment. Special retractors, needle holders, and forceps are unnecessary and serve only to complicate a relatively simple procedure. We have avoided the use of coagulation for bleeding, relying solely on the suture and ligature method when indicated.

The bladder is completely evacuated by urethral catheterization immediately prior to operation. If an indwelling catheter is in place, all the urine is allowed to run out and the catheter is removed.

1) *Position of the patient.* The patient lies in the supine position. The operator stands on the left side. Exposure of the prostatic urethra is greatly enhanced if the pelvis is elevated. This may be accomplished by the use of a sandbag or by placing the patient on the operating table so that the elevator, commonly used as a kidney or gallbladder rest, is at approximately the same level with the symphysis pubis. Raising the elevator to its maximum height or placing a sandbag under the hips at this level will elevate the lower portion of the pelvis so as to bring the prostatic urethra anteriorly and facilitate its exposure (fig. 2, *A*). By means of this maneuver, the symphysis is raised, opening up the space of Retzius. This technique actually provides more room in which to work and makes the approach a much more direct one. The increased exposure is nicely demonstrated if the elevator is dropped at the completion of the operation and the prostatic urethra will be seen to fall away from the field. It is felt that the elevation of the pelvis is a necessary step in the operative procedure. We have found it unnecessary to place the patient in the Trendelenberg position and thus minimize respiratory or cardiac embarrassment.

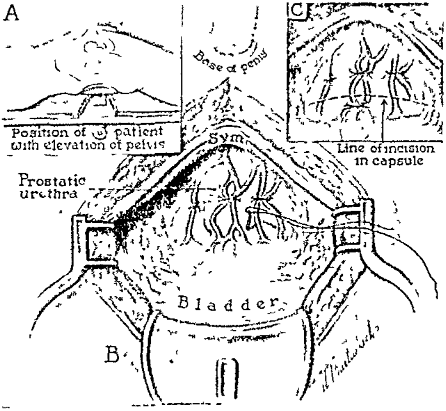

A
Position of patient with elevation of pelvis
Base of penis
C
Line of incision in capsule
Prostatic urethra
Sym
Bladder
B

FIG. 2. *A*, Pelvis raised with elevator so as to facilitate exposure of prostatic urethra *B*, Prophylactic suture-ligature of anterior prostatic plexus of veins. *C*, Transverse incision through prostatic capsule just below vesical neck.

2) *Abdominal incision.* A very low midline incision is made, starting from a point about 1 cm. proximal to the base of the penis and extending upward toward the umbilicus for a distance of 8 to 10 cm. It is essential that the lower end of the incision extend below the superior border of the symphysis, reaching almost to the base of the penis. With lateral retraction of the abdominal incision, this lower angle will be pulled upward over the symphsyis and will obstruct the exposure if the skin incision has not been extended low enough.

The rectus fascia is incised longitudinally down to and including its attachment to the symphysis. The recti are separated in the midline and a self-retaining abdominal retractor placed into the wound.

3) *Exposure of the prostatic urethra.* The bladder with its overlying peritoneum is covered with a wet laparotomy pad and is retracted backward by the left hand of the assistant. This hand retraction of the bladder is very important for a proper exposure and must be maintained throughout the operation except when enucleating the prostate. No other retractors are used at any time since *they are unnecessary and serve merely to crowd the operative field.* By retracting the bladder backward and upward, the prostatic urethra is pulled upward and is more easily approached.

The lateral fossa on each side of the prostatic urethra is then gently packed off with a wet laparotomy pad or sponge. This serves further to expose the prostatic urethra by stripping away much of the fatty tissue along its anterolateral borders. The laparotomy pads are removed and the prostatic urethra can be seen covered on its anterior surface by a small amount of fatty and loose areolar tissue. In some cases, this can be teased off with a tissue forceps to expose the grayish fascia lying on the prostatic capsule. However, there may be several large branches of the anterior prostatic plexus within this fatty tissue so that it cannot be retracted without troublesome bleeding. In most cases, no further manipulation of the fatty tissue should be attempted. Any resultant bleeding can be controlled immediately by suture or ligature.

4) *Suture-ligature of the anterior prostatic plexus.* The level of the vesical neck is now determined. The junction between the vesical neck and prostatic urethra is delineated by the heaped-up appearance of the prevesical fascia at this level. If this does not appear too distinct, palpation with a finger will easily demonstrate the firm prostate in the prostatic urethra with the soft, compressible bladder just above it.

Preliminary suture-ligature of the anterior prostatic venous plexus is then performed. As described previously, these vessels usually run in a longitudinal direction through the fascia which closely envelopes the prostatic capsule. Some branches are present in the fatty tissue lying on the fascia. Using a strong curved needle with No. 1 chromic catgut, a deep suture is taken in the midline approximately 1.5 cm. below the vesical neck going through the fatty tissue and fascia and into the prostatic capsule. This suture is tied and cut. A similar suture is placed in the midline just at the vesical neck. These two sutures also serve as markers between which the transverse incision through the capsule will be made. Two additional sutures are placed at the same level as the first suture, one at each anterolateral aspect of the prostatic urethra (fig. 2, *B*).

This general plan for prophylactic control of bleeding from the prostatic plexus is not to be followed inflexibly If any vessels are seen on the anterior surface of the prostatic urethra which would not be included in these sutures, they should be sutured separately

The routine preliminary suturing of the anterior prostatic plexus serves to keep bleeding at a minimum and saves much time and effort as the operation progresses If this is done properly, no further ligation of bleeding vessels is usually necessary during the remainder of the procedure

5) *Incision of the prostatic capsule* A transverse incision is made with a scalpel just below the level of the vesical neck The incision should be approximately 2 5 to 3 0 cm in length and pass between the two midline sutures previously placed to control bleeding (fig 2, *C*) As the capsule is incised, some bleeding will occur from its cut surfaces This is usually a venous ooze and the field is easily kept dry by means of a suction tip which is kept in the line of incision The incision should extend into the lumen of the prostatic urethra between the lateral lobes

As mentioned previously, the capsule is rather thick, about 1 0 to 1 5 cm , so that a deep incision is necessary Inasmuch as the lateral lobes usually project anteriorly, the deepest portion of the incision should be confined to the midline in order to enter the prostatic urethra

A finger is then inserted through the incision into the bladder and the upper or proximal flap of the incision grapsed with an Allis forceps The lower or distal flap is also grasped with an Allis forceps If any bleeding vessels are seen along the edges of the incised capsule, they can be clamped and ligated but this is rarely necessary

The two flaps of the capsule are retracted with the Allis forceps and the hypertrophied prostatic lobes can be easily seen (fig 3, *A*) A guy suture consisting of a full length chromic No 1 catgut is place through the midline of the lower flap This is not tied but is left long to serve as a retractor in place of the Allis forceps which is removed The purpose of the long length will be apparent later when the capsule is closed

6) *Enucleation of the prostate* A finger is now inserted into the prostatic urethra and the Allis forceps on the upper flap is removed Likewise, the assistant's hand which has retracted the bladder is removed The enucleation should always be done from below upward, i e , from the apex of the gland toward the vesical neck One lateral lobe is separated from below upward so that it is held only at the vesical neck It is then delivered through the capsular incision into the wound and held with a forceps (fig 3, *B*) The other lateral lobe is separated and delivered in the same manner The median lobe, when present, is enucleated similarly and delivered The entire prostate is then held up with forceps and its attachment to the vesical neck is cut with a curved scissors (fig 3, *C*)

If the prostate is relatively small, all of the lobes may be enucleated and delivered simultaneously Larger prostates are best removed by the method described so as not to tear the capsular incision when delivering the gland

The minimal amount of bleeding from the prostatic bed following the enucleation is striking. It is easily controlled by inserting a stick sponge into the bed and exerting pressure for several minutes. The suction tip is then placed into the bed and is sufficient to keep the field dry so that a visual inspection may be accomplished.

The entire prostatic bed should be carefully palpated for the presence of small adenomata or missed prostatic tissue. These can be easily enucleated when present. The upper and lower flaps are now retracted and the prostatic bed is examined visually for tags of mucous membrane. Any such tags are grasped with a forceps and excised with a curved scissors. This is an important step and will minimize postoperative pyuria and frequency which may be due largely to these avascularized tags producing a chronic infection.

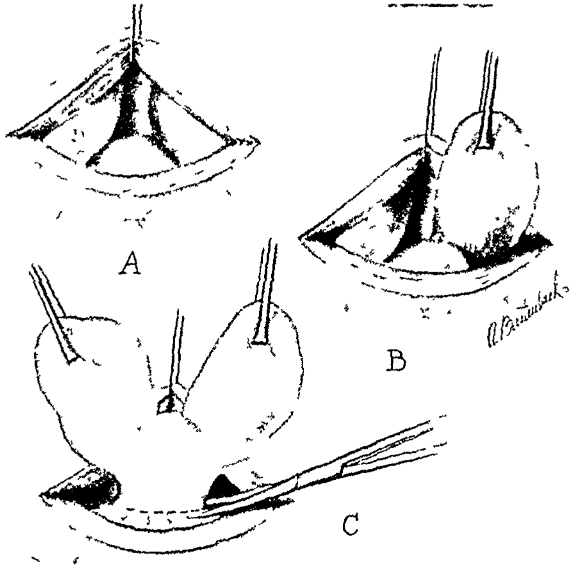


FIG. 3. *A*, Lobes of hypertrophied prostate exposed through capsular incision. *B*, Right lateral lobe delivered through capsular incision after enucleation. *C*, Lateral and median lobes have been enucleated and delivered. Attachment to floor of vesical neck is being cut with scissors.

7) *Excision of vesical neck.* Following any open prostatectomy, there is commonly a ridge or posterior commisure remaining at the floor of the vesical neck. If not adequately treated, this can be the cause of urinary retention following an apparently complete prostatectomy. The occasional persistence of urinary symptoms and residual urine after suprapubic prostatectomy is probably due to this ridge which has not been adequately removed. This ridge or bar is easily seen during retropubic prostatectomy since the vesical neck can be examined under direct vision. The ridge is grasped with two Allis forceps in the midline and is pulled up into the wound. A moderate sized wedge in the shape of a U is resected from the ridge in the midline (fig. 4, *A*). The size of the wedge to be resected can be determined by the relative amount of obstruction that the ridge produces. This will be seen to vary considerably. The wedge resection will prevent the possibility of any subsequent vesical neck obstruction

or stricture formation. Any bleeding points from the cut edges of the vesical neck may be clamped and ligated but this is rarely necessary.

8) *Insertion of catheter.* A straight Nelaton cather, 22 F. is now passed into the urethra after exposing the penis. The catheter should have an extra hole cut into it about one inch from the end in order to insure proper drainage. As soon as the catheter is seen entering the prostatic bed, it is grasped with a forceps and guided into the bladder. The end of the catheter is then sutured to the frenulum or prepuce with black silk to prevent its withdrawal.

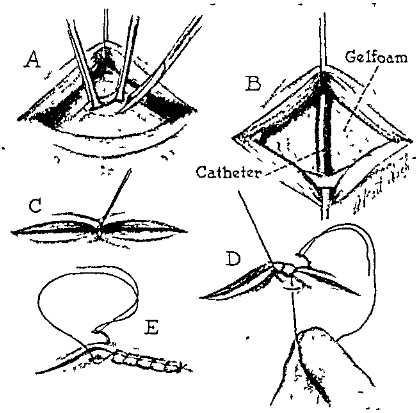


FIG. 4 *A*, Excision of wedge from floor of vesical neck. *B*, Indwelling urethral catheter in place. Prostatic bed filled with Gelfoam sponge. *C*, Upper and lower flaps of incised capsule closed in midline with original guy suture. Ends of suture left long. *D*, Begin- [illegible] half of capsular incision with continuous locking suture, using one end [illegible] *E*, Closure of right half of capsular incision completed. Be- [illegible] with continuous locking suture, using other end of midline suture.

The prostatic bed is packed firmly and completely with several pieces of large size (No. 100) Gelfoam sponge.[2] This is best done by breaking a single package of the Gelfoam into thirds and inserting the pieces into the prostatic bed, under and alongside the catheter until the entire bed is filled (fig. 4, *B*). With larger prostates, two or three packages of Gelfoam may be necessary. This serves very well to control any slight oozing that may be present.

We have considered the advisability of using a Foley bag catheter instead of the conventional straight catheter. However, with the use of Gelfoam in the prostatic bed, the straight catheter has, thus far, been satisfactory and provides better drainage. It is possible that with increasing experience, a Foley bag catheter may be preferable.

9) *Closure of capsule.* The original guy suture of a full length, chromic No. 1

---

[2] The Gelfoam used in this study was supplied by The Upjohn Company, Kalamazoo, Mich.

catgut which was placed through the lower flap for retraction purposes is used to close the capsule. One end of the suture is threaded on an empty curved needle and a bite is taken through the upper flap in the midline. This is tied, leaving both ends of the suture equal in length. The capsule is thus held together with this one suture in the midline (fig. 4, *C*).

Using one end of the midline suture on a curved needle, one half of the capsular incision is closed with a continuous locking suture going from the midline to one lateral angle of the incision (fig. 4, *D*). When this is completed, the remaining half of the capsular incision is closed in a similar manner using the other end of the midline suture (fig. 4, *E*). By means of this technique, each half of the capsular incision is more fully exposed by retraction of the midline suture in the opposite direction. The capsular closure is thereby facilitated and a practically water-tight suture line is obtained (fig. 5).

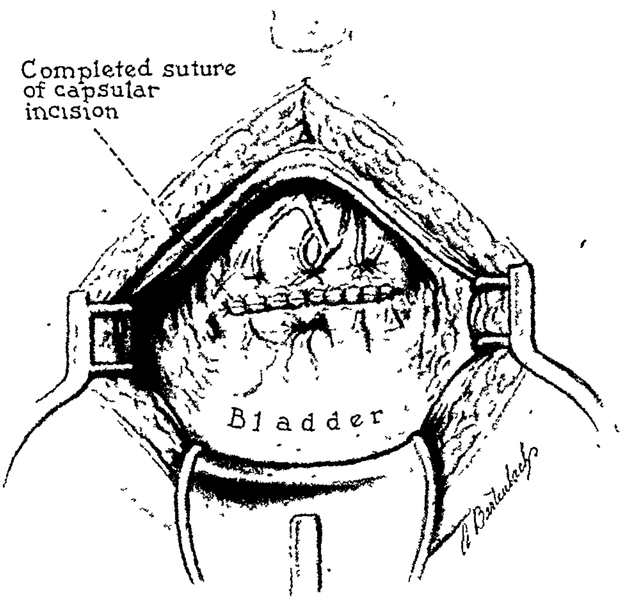


FIG. 5. Capsular incision completely closed

As soon as the capsule has been closed, the catheter is irrigated with sterile water using a bulb syringe, and the return flow is observed. Slight pressure on the bladder should cause a free flow of the water which will be a light pink color. If a slight leakage of water occurs through the closed capsule, there is no indication for further closure. However, if a definite stream of water pours through a site of faulty closure, this should be reinforced with an additional interrupted suture. When the original closure of the capsular incision has been properly performed, no further suturing will be necessary.

10) *Closure of wound.* The closed capsule and anterior plexus of veins are now examined for bleeding. The entire operative field should be perfectly dry but if any oozing is present, it can be easily controlled by clamp and ligature. A rubber Penrose drain is placed down to the capsular incision, emerging from

the lower angle of the wound. The recti are approximated by several loosely tied chromic No. 0 sutures. The fascia is closed with interrupted chromic No. 1 catgut and the skin is closed with silk.

The urethral catheter is irrigated again to check for bleeding. The return flow should be light pink in color.

POSTOPERATIVE CARE

The indwelling urethral catheter is connected to a rubber tubing and bottle and the color of the drainage is observed. Routine irrigation is not practiced but if there is any question of increased bleeding or plugging of the catheter by clots, the catheter is irrigated at regular intervals with a bulb syringe. Any clots are aspirated and the catheter is allowed to drain as before. Prolonged or severe bleeding is rarely encountered.

The catheter is removed in from 5 to 7 days. If there is no urethritis, we prefer to leave the catheter in for a full week. After removal of the catheter, the patient voids spontaneously and without difficulty.

Suprapubic urinary leakage may occur occasionally following removal of the catheter. In this event, a No. 18 Tieman catheter is reinserted and left indwelling for 2 or 3 days. We have had no difficulty reinserting a catheter when necessary. This is usually sufficient to allow the capsular incision to heal completely.

The suprapubic drain is shortened on the fourth day and removed on the sixth day. A slight to moderate amount of seropurulent material usually drains from the lower angle of the wound for about 10 days. This ceases spontaneously and the wound is usually completely healed in about 14 days.

The patient is allowed out of bed on the first or second postoperative day and every effort is made to encourage early ambulation and to avoid prolonged recumbency.

Penicillin and sulfonamides are administered routinely for 5 days postoperatively. We have seen no case of postoperative ascending pyelonephritis.

ANALYSIS OF CASES

We are reporting a series of 40 unselected patients on whom retropubic prostatectomy was performed. The first 34 of these cases were done at the Cook County Hospital, the remaining 6 were private patients at the Michael Reese Hospital.

Age and race. There were 26 white patients and 14 colored patients. The age distribution, according to decades, was as follows: 50 to 59, three patients; 60 to 69, seventeen patients; 70 to 79, eighteen patients; 80 to 89, two patients.

Condition of patients. Each patient's condition was arbitrarily classified as good, fair, or poor depending upon the nutritional status, presence of cardiovascular disease, general condition, duration of urinary symptoms, blood chemistry and blood count. Surgery was performed after adequate treatment of any co-existing disease. Urinary retention, varying in duration from several hours to 1 week occurred in 33 of the patients prior to admission. Many of these had been catheterized repeatedly on the outside. There were 8 patients classified as being in good condition, 15 as fair, and 17 as poor.

Mortality. There were 3 operative deaths in this series. The first was a 73 year old colored man in poor general condition. He was very obese, with a hypertension of 180 systolic over 120 diastolic and an enlarged heart. Blood chemistry was normal. After preoperative management it was felt that a 1-stage procedure was indicated. A retropubic prostatectomy was performed and a gland weighing 25 gm. was enucleated without difficulty. This patient was case 5 in our series and at that time we did not appreciate the importance of careful prophylactic suturing of the anterior prostatic veins. Accordingly, there was a moderate amount of bleeding from the anterior plexus following incision of the capsule. This was partially controlled after some difficulty, but a moderate amount of oozing persisted after closing the capsule. It was not thought to be serious and the patient was returned to the ward. The urethral catheter was draining blood-tinged urine but no more than was expected. About 2 hours following surgery, severe bleeding was noted coming from the suprapubic wound, completely saturating the dressing. There was some bloody drainage from the urethral catheter but no clots were present. The lower end of the suprapubic wound was quickly opened and a gauze packing was inserted into the space of Retzius. A large amount of blood was evacuated upon opening the suprapubic wound. The patient went into shock quickly in spite of whole blood and plasma infusions. He died about 3 hours postoperatively.

Postmortem examination revealed evidence of marked hemorrhage in the space of Retzius with some extension of the blood into the retroperitoneal tissues. No large blood vessels could be seen which would account for the hemorrhage but this would normally be difficult to demonstrate. Both the bladder and the prostatic bed appeared clean and did not contain any blood clots.

On the basis of the clinical picture and the postmortem findings, it was felt that a severe hemorrhage from the anterior prostatic plexus of veins precipitated a condition of irreversible shock with a resultant mortality.

The second mortality occurred in a 72 year old white man whose preoperative work-up was essentially normal. There was a history of slight dyspnea on exertion and the electrocardiogram showed changes compatible with his age. A retropubic prostatectomy was performed in the usual manner without difficulty and a benign hypertrophied prostate gland weighing 66 gm. was removed. The postoperative course for the first 4 days was entirely uneventful. On the fifth day, the patient complained of severe chest pain and marked shortness of breath. Pulmonary edema supervened in a few hours and in spite of oxygen and supportive therapy he expired the same day. The clinical impression was an acute left ventricular failure with pulmonary edema. Permission for a postmortem examination could not be obtained.

The third mortality occurred in a 70 year old colored man upon whom a cystotomy had been performed 6 weeks previously because of chronic urinary retention and very poor general condition. Blood chemistry studies and cardiac status were essentially normal. His general condition had improved sufficiently to warrant a second stage procedure. A retropubic prostatectomy was performed after resecting the fistulous tract from the bladder. This was done without too much difficulty and the entire procedure consumed a total of 50 minutes. The cystotomy opening was closed with several interrupted catgut sutures.

Several complications developed during the postoperative course. Marked adynamic ileus appeared on the second day and persisted in spite of intestinal decompression. On the sixth day, the suprapubic wound broke down and the cystotomy wound reopened, draining urine and purulent material. The patient was treated with intravenous fluids, plasma and whole blood and was given adequate doses of antibiotics. However, he ran a progressively downhill course and expired 13 days postoperatively with a terminal bronchopneumonia. Permission for a postmortem examination could not be obtained.

In this case, the outcome would have probably been more favorable if the original cystotomy fistula had not been resected out and closed. The additional trauma involved in a poor risk patient, may have been sufficient to initiate the local breakdown and infection of tissue and the development of an adynamic ileus.

In the remainder of the cases, a very careful prophylactic suturing of the anterior prostatic plexus of veins was performed. Before closing the abdominal incision, the operative field was examined for any possible bleeding points which were immediately controlled with suture or ligature. With this technique, no bleeding of any consequence from the anterior plexus of veins was encountered in any other case.

Postoperative shock. The shock-like picture occasionally seen after suprapubic prostatectomy or transurethral resection was noticeably absent in this series. Following retropubic prostatectomy, the patient appears in a state of well-being and does not exhibit any evidence of undue surgical trauma.

Morbidity. Nine patients had temperatures of 101 F. or above during the postoperative period. In 3, epididymitis was present which probably accounted for the high temperature. In 1 patient, a small gland was removed which proved to be a carcinoma of the prostate. It was enucleated with some difficulty and the trauma was undoubtedly a factor in the febrile course. His temperature varied from 102 to 103 F. for several days and then gradually subsided. The other 5 patients had temperatures of 101 F. and 102 F. for 48 hours postoperatively which then subsided.

All but 6 patients were discharged from the urological service between the eleventh and fourteenth day postoperatively. One of these began to drain a slight amount of urine suprapubically on the twelfth day. A urethral catheter was inserted and left indwelling for 3 days following which he remained dry above. He was discharged on the nineteenth day. Three patients developed epididymitis postoperatively on the seventh, eighth, and eleventh days respectively. They were discharged from the hospital on the sixteenth day. One patient was kept in the hospital for 30 days because of a persistent urinary fistula. ✓This was the patient in whom the pathological report was adenocarcinoma of the prostate.

One patient was re-admitted several weeks after discharge because of a periostitis pubis. He was kept in the hospital for almost two months until subsidence of all symptoms.

Many of the patients could have been discharged earlier but in view of their poor general condition, it was felt that an increased period of observation was advisable.

Hemorrhage. As mentioned previously, there was 1 case of severe hemorrhage from the anterior prostatic plexus which resulted in a fatality. In no patient did severe postoperative hemorrhage occur from the prostatic bed or vesical neck. In approximagely one-third of the patients, intermittent irrigation of the urethral catheter for the first 24 hours was necessary to maintain the patency of the catheter. Suprapubic cystotomy or transurethral fulguration was never necessary to control bleeding.

Secondary bleeding occurred to a moderate degree in 5 patients between the eighth and eleventh days postoperatively. This was easily controlled with an indwelling catheter for 24 hours in each case. Late bleeding occurring after discharge from the hospital has not been encountered thus far in this series.

Suprapubic urinary fistula. Suprapubic urinary drainage occurred in 9 patients. Four of these patients had a postoperative indwelling catheter for only 4 days. In the 5 remaining cases, the catheter had been left in for 6 or 7 days. In all 9 patients, a catheter was reinserted for 48 hours and no further leakage occurred.

A relatively persistent suprapubic urinary fistula occurred in 1 patient in whom the pathological report of a small gland revealed adenocarcinoma. He was discharged from the hospital on the thirtieth postoperative day leaking only very slightly. Weekly urethral dilatation for 1 month was effective in closing the fistula completely.

Suprapubic drainage. A mild to moderate degree of seropurulent drainage from the lower angle of the wound occurred in every case. This was occasionally mixed with dark blood probably due to a slight ooze from the anterior plexus of veins. The drainage spontaneously ceased and all wounds were healed by the fourteenth to twenty-first day.

Pyuria. Clear or slightly hazy urine by the fourth to sixth postoperative week was seen in almost all cases. In several instances, the urine remained cloudy for 6 to 12 weeks. Cystoscopy patients revealed tags of mucous membrane producing a slow slough as a cause for the pyuria. All of these eventually cleared up.

Urinary frequency. The short duration of postoperative diurnal and nocturnal frequency was in sharp contrast to the usual picture after transurethral resection. Nocturia of once or twice within 3 to 4 weeks after retropubic prostatectomy was the usual findings. Within 8 weeks urinary habits were within the range of normal in this age period.

In 1 patient, urinary frequency and urgency persisted, together with a residual urine of 300 cc. Cystoscopy revealed a small adenoma causing obstruction at the vesical neck. This had been missed at the operation. This was resected transurethrally with subsidence of symptoms and residual urine. A more careful examination at the time of surgery would have revealed this adenoma which should have been enucleated. This case demonstrates the importance of a careful search for a small adenomata when enucleating the prostate.

Stricture. There was no instance of postoperative stricture of the urethra or vesical neck. In most of the cases sounds were routinely passed 6 weeks postoperatively with a 26 F. and then at biweekly intervals for 2 months.

Epididymitis. There were 3 patients who developed epididymitis postoperatively. In each case the epididymitis subsided with the usual treatment. Preliminary vasectomy was not performed on the patients in this series in order to determine the incidence of epididymitis without prophylactic vas ligation.

Periostitis pubis. This occurred in one of the earlier patients in the series. At that time we were using Deaver retractors in the lateral fossa on each side of the prostatic urethra. The trauma to the rami of the pubis due to the constant pressure of the retractors may have been a contributing factor in the development of the periostitis. We have since discarded the use of these retractors.

This patient developed the typical signs and symptoms of periostitis pubis 5 weeks postoperatively. The diagnosis was confirmed by x-ray of the pelvis. He improved gradually over a period of 6 weeks on bed-rest and left the hospital in good condition.

Pelvic cellulitis. Inasmuch as there is a variable amount of seropurulent drainage from the lower angle of the suprapubic wound in every patient, some degree of infection in the space of Retzius must necessarily be present. In the series reported, however, we did not encounter any instance of diffuse retroperitoneal cellulitis associated with high fever and toxicity.

Miscellaneous complications. Urinary incontinence, urinary retention, ascending pyelonephritis, pelvic thrombosis, or pulmonary embolism did not occur in any patient.

DISCUSSION

The fundamental soundness of any operative procedure is best determined by its application to a series of unselected cases in a large charity hospital. The patients admitted to the urological service of the Cook County Hospital are extremely poor surgical risks and have very little reserve to withstand any undue surgical trauma. Their nutritional status is far below normal and the incidence and degree of pulmonary and cardiovascular disease is much greater than is seen in private practice. As a rule, these patients seek admission to the hospital only after the symptoms of prostatism have existed for a long time and the resultant pathologic physiology has reached a late stage. This adds materially to the risk of any operative procedure which is performed. Thirty-four of the patients in this series were from the Cook County Hospital and presented the usual complicating factors.

In view of these facts, the smooth operative and postoperative course of our patients undergoing retropubic prostatectomy is very striking. The aged and poor risk patient tolerates this operation very well, there being no evidence of shock either during or immediately following the procedure. This is probably due to three facts: 1) The operation is performed deep in the pelvis, being essentially a perineal procedure performed from above. 2) The bladder is not opened and the bladder neck is not traumatized or divulsed in order to enucleate the prostate, as is done in the suprapubic approach. 3) There is very little bleeding from the prostatic bed. The most probable explanation for the minimal degree of bleeding is the fact that the enucleation is performed from the apex or distal end of the hypertrophied gland up toward the vesical neck. The attachment of the prostate to the vesical neck is very firm and is cleanly severed with a dissecting scissors rather than torn with the enucleating finger. Using this technique, the vesical neck with its rich supply of blood vessels is not traumatized and bleeding is kept at a minimum. Any slight oozing that may occur in the prostatic bed is adequately controlled by firmly packing the entire bed with pieces of large size (No. 100) Gelfoam sponge.

Retropubic prostatectomy is an anatomical procedure in the true sense of the word. Exposure and visualization of the operative field are far more satisfactory than in any other operation on the prostate. The prostatic bed and vesical neck can be carefully examined both digitally and visually for possible missed adenomata and in order to control bleeding. With the proper technique, the prostatic urethra is easily accessible so that a minimum of trama accompanies the enucleation of the gland.

It is not a difficult procedure to learn, requiring far less experience than the perineal or transurethral operations. Once the technique has been mastered, the duration of the operation should not exceed 30 or 35 minutes. There is no danger of injury to important adjacent structures which is an ever-present hazard in the other procedures. Practically the sole possible source of bleeding is from the anterior prostatic plexus of veins. This is easily prevented by careful suture-ligature of the vessels prior to incising the capsule. If some bleeding does occur from this site, the exposure allows the operator to suture or ligate any bleeding points without difficulty.

Exposure of the prostatic urethra is facilitated in direct proportion to the size of the hypertrophied gland. Inasmuch as the distal point of the prostatic urethra, i.e., the triangular ligament, is a fixed structure, the prostate must necessarily enlarge towards the vesical neck or bladder. As a result, the prostatic urethra is lengthened in a proximal direction up into the pelvis and away from the symphysis. Thus, the large sized glands are higher in the pelvis and may be approached with greater ease than the smaller glands. The operation is ideally suited for the larger sized glands which would be too difficult and time-consuming to resect transurethrally.

After the prostate has been enucleated, the transverse capsular incision usually appears somewhat longer than when it was originally made. It was thought at first that this incision might have been torn while enucleating the prostate. However, on making the incision, a suture was placed at each end to serve as a marker. Following the enucleation of the prostate, the incision seemed longer but the ends of the incision could be seen in the same relationship to the suture markers as formerly. This indicates that there is no further traumatic extension of the incision but that the incision is lengthened due to the marked mobility of the prostatic capsule after its firm attachments to the prostate are no longer present. The very intimate adherence between the capsule and the prostate maintains the capsule in a fixed position and allows for little or no mobility. After the removal of the prostate, the capsule is no longer fixed and becomes very elastic and mobile. This is further evidenced by the increased mobility of the upper and lower flaps of the capsule following the enucleation.

Cystoscopy in most of these patients has been done about 6 to 8 weeks postoperatively. The prostatic bed appears clean and somewhat distorted. It is interesting to note that the lumen of the prostatic urethra becomes considerably smaller even after the enucleation of large glands. Apparently the prostatic capsule collapses after the supporting gland has been removed, so that the width of the lumen becomes more compatible with the normal. Occasionally, loose tags of mucous membrane can be seen which are partially avascularized and may account for the presence of pyuria. In 2 cases, very small adenomata were visualized along the lateral wall of the urethra which were missed at operation. Since they were not in a position to cause obstruction, no further procedure was advised. In 1 case, a missed small median adenoma actually caused a partial obstruction at the vesical neck necessitating a secondary transurethral resection.

Our experience with postoperative cystoscopy has emphasized the importance of thorough examination of the prostatic bed for loose mucous membrane tags and small adenomata. These should be completely removed at the time of operation.

The actual technique of retropubic prostatectomy is not difficult and requires no special equipment if the following important details are observed:

1) Elevation of the pelvis.

2) Extension of the lower end of the abdominal incision practically to the base of the penis.

3) Continual retraction of the bladder backward and upward by the assistant's hand.

4) Prophylactic suture-ligature of the anterior prostatic plexus of veins.

5) Enucleation of the prostate from the distal end or apex up toward the vesical neck.

6) Excision of a wedge from the floor of the vesical neck.

7) Use of a guy suture through the lower flap of capsule for closure of capsular incision.

The incidence of postoperative complications, although not large, is sufficient to warrant continued efforts to modify the operative procedure in an attempt to further reduce these complications. Suprapubic urinary leakage seems best controlled if the indwelling urethral catheter is maintained for at least 1 week. We have not observed any stricture formation or incisional hernias but the follow-up in our series has not been long enough to make a definite statement as to these possibilities. Severe postoperative hemorrhage from the prostatic bed or vesical neck has not occurred as yet. It is felt, however, that this ever-present bugaboo of all prostatic surgery will appear after a sufficient number of cases have been performed.

The control or elimination of infection in the space of Retzius is a problem which will require further study. That some degree of infection in this area occurs is evidenced by the invariable appearance of seropurulent drainage in every patient. It is not unlikely that this may occasionally develop into a spreading cellulitis in spite of the routine use of a Penrose drain in the space of Retzius. A definite abscess formation in the space of Retzius occurred in one patient who had a retropubic prostatectomy performed during the preparation of this publication. This patient had a low-grade fever starting on the fourth postoperative day. The lower angle of the wound was probed and an abscess cavity was opened on the sixth day. His further course was uneventful. The routine use of sulfanilamide powder in the space of Retzius, as practiced by Millin, may have a definite value in preventing infection. We have also considered the possibility of making a stab wound through the perineum on each side of the prostatic urethra in order to provide for dependent drainage of the space of Retzius. It is planned to try this procedure in the future.

CONCLUSIONS

Retropubic prostatectomy is a sound surgical procedure and merits further trial and study to establish its proper place in the field of prostatic surgery.

A detailed description of the operative technique, modified after Millin, is presented.

The mortality, morbidity and postoperative complications in a series of 40 unselected cases are analyzed.

104 S. Michigan Ave., Chicago, Ill.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

RETROPUBIC PROSTATECTOMY: REPORT OF 102 CASES[1]

SAMUEL K. BACON

From the Department of Surgery (Urology), University of Southern California School of Medicine, Los Angeles

It is remarkable to note the tremendous interest in retropubic prostatectomy since its presentation by Terence Millin of London. Many American urologists are utilizing these principles, but, in spite of this enthusiasm, we must proceed cautiously.

An outline of the technical steps and pictorial display of the operation may, erroneously, give an exaggerated simplicity to this surgical procedure. To avoid misapplication of the technique, we should frequently take inventory of results.

In earlier papers I have presented the historical background of retropubic prostatectomy, features of the operation, surgical technique, and my clinical experience in the management of 32 cases.

The successful conduct of retropubic prostatectomy is dependent on anatomic knowledge of the space of Retzius. This should be obtained on the cadaver before actual clinical application of the operation. Strict adherence to the principles of surgery will minimize any complexities. Features of particular significance in obtaining surgical proficiency are: proper exposure of the retropubic space, gentle dissection, maintenance of a dry field, excision of a posterior section of tissue from the vesical neck, thorough hemostasis, and adequate repair of the prostatic capsule.

The most useful purpose of this extravesical procedure is for complete excision of large or medium adenomatous hyperplasias, though all types of prostatic obstruction have been approached in the retropubic area. From the patient's point of view the operation has the advantage of affording increased comfort during convalescence, prompt urinary control and preservation of sexual potency.

Within the past year retropubic prostatectomy has been carried out on 102 cases: 87 from the County Hospital, and 15 patients from private practice. During this period other types of prostatectomy carried out were: 265 endoscopic, 63 suprapubic, and 23 perineal.

The patients comprising the private group were carefully selected as to risk and pathologic lesion. Results obtained were excellent; no mortality or significant complication, average voiding on the sixth postoperative day, and discharge from the hospital on an average of 8.2 days. On the other hand, County Hospital patients were unselected except for the general factor that prostates were enlarged and obstructing vesical outlets. The majority had severe infection of the urinary tract and were poor surgical risks. Before surgery they were subjected to indwelling urethral catheter drainage, chemotherapy, penicillin, general supportive measures, and adequate urologic studies. Because of an institutional restriction streptomycin was not available. Including several resident physicians, at least 19 urologists participated in the surgery program.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

The oldest patient was 96 years of age, and the youngest was 51; 53 per cent were between the ages of 70 and 96; 11 patients were past their eightieth year. The average age, in this series, was approximately 74 years.

Cases	*Years*
9	51–59
39	60–69
43	70–79
10	80–89
1	96

The initial emergency in 75 per cent was complete retention of urine. In 89 cases the urine was moderately or severely infected. General physical and special examinations revealed a remarkable incidence of cardiorenal-vascular disease with hypertension. Occasionally a history of coronary occlusion was elicited. Other lesions occurring and frequent findings of preoperative importance were: hematuria, anemia, pneumonia, diabetes, hemiplegia, urethral stricture, vesical diverticula and urinary calculi.

Six specimens were malignant. The largest prostate weighed 190 gm., and the smallest weighed 6 grams:

Cases	*Weight in gm.*
4	6– 19
20	20– 39
42	40– 69
36	70–190

The mortality rate in this series of 102 cases was 6.8 per cent. Four patients expired suddenly as a result of coronary occlusion (2 on the day of operation and the other 2 on the second and fourth postoperative days). Another sudden death followed cerebral hemorrhage on the fifth day. Following a pulmonary embolism the sixth patient expired on the sixth day. Another patient, who bled profusely after surgery, became septic and markedly debilitated, and death occurred on the thirty-third day postoperatively.

Postoperative hospitalization averaged 17.1 days. This long stay was materially influenced by the fact that the majority of these patients were poor surgical risks. Urinary leakage through the capsule, wound infection, hemorrhage, and the lack of uniform operative dexterity among the 19 surgeons (although not predominating circumstances) obviously accounted for many additional days of hospitalization.

In 6 instances, during the immediate period following operation, severe hemorrhage occurred. This complication was generally attributed to improper hemostasis at surgery. Secondary hemorrhage was essentially insignificant except on the fifteenth day in 1 case, and endoscopic fulguration of an artery effected prompt hemostasis.

Excising a posterior section of tissue from the bladder neck was not routinely practiced in this series, and consequently, resulted in contracture of the vesical neck which necessitated endoscopic resection or division with a diathermy knife in seven instances.

Finally, the devil had a field day when one of the patients developed osteitis pubis! According to the record of this traumatizing operation, with gross inexperience, unestablished technical maneuvers were attempted! During the postoperative period urinary leakage occurred, severe wound infection and pneumonia ensued. In spite of all this the patient completely recovered, and was discharged from the hospital on the thirty-fifth postoperative day.

SUMMARY

The urologic surgeon must proceed cautiously when utilizing principles of the retropubic approach.

As a preliminary consideration, and before actual application of the operation, investigation of the space of Retzius on the cadaver is suggested.

This operation has advantage of affording increased comfort during convalescence, prompt urinary control and preservation of sexual potency.

The most useful purpose of retropubic prostatectomy is for the complete excision of large or medium hyperplasias.

In order to avoid misapplication of this technique to prevailing lesions, it is urged that an inventory of results be frequently considered.

One hundred two cases of prostatectomy by retropubic approach are reported, pertinent clinical details given, and features of particular significance in obtaining surgical proficiency are described.

1680 N. Vine St., Hollywood 28, Calif.

REFERENCES

Bacon, S. K.: Retropubic prostatectomy: An extravesical technique; report of 32 cases. J. Urol., 59: 376, 1948.

——: Discussion of retropubic prostatectomy by Terence Millin. J. Urol., 59: 276, 1948.

——: Retropubic prostatectomy: Early technical difficulties. Report of removal of giant prostate. In press, J. Urol.

Bacon, S. K.: Surgical technique of petropubic prostatectomy: An extravesical operation. Trans. South Central Sect. A. U. A. pp. 77–82, 1947.

Lowsley, O. S. and Gentile, A.: Retropubic prostatectomy. J. Urol., 59: 281, 1948.

Millin, T.: Retropubic prostatectomy: New extravesical technique. Report of 20 cases. Lancet, 2: 693, 1945.

——: Retropubic Prostatectomy. Proc. Roy. Soc. Med., 39: 327, 1946.

——: Retropubic Urinary Surgery. Baltimore: Williams and Wilkins Co., 1947.

——: Retropubic prostatectomy. J. Urol., 59: 267, 1948.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

DISCUSSION

MR. TERENCE MILLIN (London, England): Dr. Bacon is to be congratulated on his timely presentation. Himself a keen proponent of retropubic prostatectomy, he has indicated the difficulties and the ill results that can and will follow the operation carried out by those not trained in, or fully conversant with, the technique. It recalls the paper of Dr. Alcock in the early days of transurethral resection.

Having heard of a number of modifications in the technique which had been introduced, I came here this year hoping to learn of some valuable addendum to our technique, for there is no operation which cannot be improved. I have been disappointed. The three beautiful films which we saw yesterday either failed to show certain points which we regard as cardinal in the technique, or portrayed what we have come to regard as gross errors.

If you hope to obtain good results in any operation you must perform the technique correctly and so I feel that several points require further stressing.

1) A short transverse incision of skin and aponeurosis immediately above the pubis with midline separation of the recti will give adequate room, and you will leave a sound abdominal wall. I see no need for incisions from Dan to Beersheba either longitudinal or that barbaric Czerny variety.

2) Be gentle throughout the operation. This should not be a traumatic avulsion of the adenoma through a capsular hole instead of a transvesical one. Careful exposure of the anterior aspect of the capsule, a short 2 cm. transverse incision of the same 1 cm. below the bladder neck will give in most cases an adequate exposure of the adenoma and allow a gentle enucleation, either digital or instrumental. Enucleation should invariably be preceded by a deliberate sectioning of the urethra immediately distal to the apices of the lateral lobes. In this way the risk of avulsion of any of the membranous urethra is well-nigh eliminated. A preliminary injection of the gland with 20 cc of 1 per cent procaine containing ½ cc pitressin will give an almost bloodless field. (In 25 consecutive cases the average blood loss was 80 cc.) The vertical incision of the capsule I have little use for. It has been tried by many of us in Europe and found wanting. There is the risk of the incision splitting downwards and leading to involvement of the compressor, or upwards and so encroaching on the bladder neck. When the latter occurs either accidentally or by deliberate section, an advocated yesterday by one film exhibitor, the procedure is no longer extravesical and subsequent suturing of the bladder neck is called for. This spells fibrosis and probable stenosis at this danger point in all prostatic surgery.

3) I would impress again the absolute necessity of a careful toilet of the vesical neck. If there is the least suggestion of stenosis at this region excise a generous portion of the posterior lip, preferably subepithelially and then draw down the apex of the trigonal mucosa, fixing it to the floor of the prostatic fossa rather after the manner of Harris's retrigonization suture. If you do that you will not have subsequent late stenoses. None of the films demonstrate this important step.

4) Hemotasis. This is effected by pinpoint coagulation. Surely a cardinal

rule of surgery is to pick up bleeding points and seal them by ligature or coagulation and not rely as a routine on artificial hemostatics as oxidicised celloidin. The routine use of this or similar coagulants popular today, I condemn as being unnecessary and not without serious disadvantages, well known to you. It is usually possible to underpin the prostatic arteries with a suture and so avoid all risk of serious secondary haemorrhage.

5) The capsular closure should be completely hemostatic and watertight. No method of interrupted suturing will effect this. A carefully applied continous suture of No. 1 chromicized catgut will enable the patient to pass urine without leakage within a few hours of the operation. Modern prostatic surgery calls, we believe, for a minimum period of artificial drainage. We aim at removing the catheter on the first, second or third postoperative day, unless the bladder is atonic. The septic complications are minimized. The best drainage of the nonobstructed bladder is normal micturition. We do not wait for the urine to be completely free of blood. Once all active hemorrhage has ceased the catheter can be safely withdrawn, if the capsular suturing has been correct. Exceptions will, of course, be made where urinary infection has not been completely controlled before operation. In a properly conducted operation there should be no difficulty in reintroducing the catheter should such become necessary. Recently, one of my assistants had the following experience. The patient, 10 hours after operation, removed his catheter and voided naturally; he then took fright and, without asepsis, lubricant or difficulty, replaced the catheter himself.

We have now completed almost 600 cases. Our overall mortality, including a high proportion of charity cases, has been 4.75 per cent. In those under 70 years the mortality has been less than 2 per cent, a figure which we have not been able to secure with transurethral resection, and we have the satisfaction of knowing that the obstruction has been completely and permanently removed, which is certainly not the case in our resections. Do not think that we have abandoned the transurethral route. We use it in the nonagenarians and some others!

DR. C. D. CREEVY (Minneapolis, Minn.): I approach this discussion with humility, because my experience with retropubic prostatectomy is limited and not to be compared with that of the previous discussants.

I should like to ask a question of Dr. Bacon and of Mr. Millin. Why do they elect to make the incision for enucleation of the prostate in the capsule, which is the most vascular portion of the lower urinary tract, when it can be done as readily in the far less vascular bladder, thus saving a lot of blood? I have recently tried on a number of occasions making the incision in the midline of the anterior wall of the bladder, beginning about 1½ inches above the prostate and ending at its margin. The gland is then enucleated from above by whatever method the operator prefers. Hemostasis can be secured in the same manner as with the operation of Mr. Millin. It is made a little more secure by lining the prostatic fossa with Oxycel gauze and by inflating a Foley balloon catheter in the fossa in order to maintain contact with the oxycel. A small (14 F.) mushroom catheter is brought out through a separate puncture in the bladder and abdominal wall and the original incision is closed tightly.

An additional point with this method is that a much more satisfactory closure can be made in the incised wall of the bladder than in the friable, vascular prostatic capsule.

The point I really wish to make in this discussion is to point out that, given an urologist who is adequately trained, who has the necessary patience—spelled "c-e"—and has a strong enough back, I still feel that transurethral resection is the operation of choice for the average case of prostatism. The convalescence is more comfortable, the period of hospitalization is shorter, the risk to life is measurably less, and I have not yet seen it followed by osteitis pubis, prevesical abscess, or suprapubic fistula.

If I found that my prostate is beginning to trouble me, I will seek out a first class resectionist.

DR. GERSHOM J. THOMPSON (Rochester, Minn.): I rise first to compliment Dr. Bacon on his very able presentation of his experience with retropubic prostatectomy. I am glad that he has called attention to some of his adverse experience for that is what you gentlemen who are about to embark on your first voyage through the plexus of Santorini are interested in. I too have tried the operation and had a perfect result, the patient healed per primam and had no complication of any kind, so that my experience in this 1 case was 100 per cent.

As I viewed the motion pictures yesterday and in spite of the technical excellence of Dr. Bacon's movie and of the others, I was impressed with the bleeding encountered and by the relatively poorer visualization one had with the retropubic approach than was the case with the 1-stage visualized transvesical suprapubic prostatectomy which the late Dr. Verne Hunt perfected. He performed 200 consecutive primary prostatectomies without a single death but in a larger series of cases the mortality rate was around 5 per cent. He did this operation under full vision and with accurate control of bleeding. The fact that he cut through the bladder wall to do it instead of through the prostatic capsule is the only difference that I can see in contrast to the operation which Dr. Bacon and Mr. Millin are now advocating.

At the Mayo Clinic we developed and have continued to employ transurethral prostatic resection because we believe that it is a safer operation for the poor risk patient. Our experience with the transurethral procedure leads us to believe that it is still the operation of choice for prostatic obstruction in practically all patients. In the last 100 cases in 1947 our mortality rate was 1 per cent; in 1,110 cases in 1947 it was 0.9 of 1 per cent. In the past 10 years in 11,522 unselected cases the mortality rate has been 1.2 per cent.

In the face of this experience we have been reluctant to select cases for retropubic operation. As I grow older transurethral resection does not get any easier, yet I am reluctant to do another type of operation which according to the experts carries a higher mortality than we have experienced with transurethral resection. I believe there is some virtue in this retropubic procedure but as yet I have not been convinced of its exact place in the management of the prostatic patient. I would like to hear more about the indications for the operation; what type of case should be selected for the procedure. It seems to me likely that in the larger glands requiring more than 1 stage of transurethral resection the retropubic procedure might have its place. I have removed 176 gm. of prostatic tissue in one transurethral resection and 280 gm. in two procedures but I have the feeling that in such glands some other type of operation, perhaps a retropubic prostatectomy, might be better.

In the final analysis I presume it is up to each man to do the operation which he thinks in his hands will give his patient the best result.

Dr. Owsley Grant (Louisville, Ky.): In discussing this matter with my friends, I find there is a great deal of enthusiasm and a lesser amount of criticism. I find most of the criticism stems from the possibility of hemorrhage at the time of operation and the reports of the subsequent events that have been circulated as happening postoperatively.

It is our belief that this operation is a meticulous operation, not one to be entered into readily. All of you know what it would take to do a perineal prostatectomy. You wouldn't dare venture to do that after two or three observations.

We feel if there had been as much distress as might be inferred from some of the conversation, that this operation would have died a'borning in its year of American birth, rather than have proceeded as it has to enthusiasm.

Since there is at the present time no well defined American treatise on this subject, I think that if you are having persistent trouble with the operation the only remedy is to see one or two or more of the men who are performing this operation satisfactorily. There, I believe, you will find that you are overlooking some seemingly trivial step in this procedure and that by the advice of those who have mastered it you will find that your difficulties are readily solved.

The second feature of inportance I would like to mention is: Do not try to modify this operation. The virtuoso who designed the procedure showed extraordinary forethought in protecting us from the errors into which we might fall. As a result he has devised an operation that I think needs little modification. One shudders almost to look and to hear of Oxycel packs and distended Foley catheters in the prostatic fossa, when they obviate the very purpose for which this operation was devised, namely, the prompt and early reconstruction of a normal urethra.

I have often contended at meetings of this Association that it is an utterly false philosophy that the surgeon should perform the type of prostatectomy with which he is most familiar in preference to all others, no matter what the pathological changes in the gland. Surely any surgical urologist worthy to belong to this society or the American Board of Urology should not find it necessary to fit the patient to the operation but should be capable of performing the operation best suited to the patient's condition.

We do feel however, that the retropubic operation offers the best solution for the vast majority of large glands. Having done only an humble series of 120 cases of retropubic prostatectomy we do not believe that we are entitled to draw final conclusions or that we can prophesy that this form of operation is the apotheosis of prostatic surgery but we do believe, reasoning from a long series of all types of prostatic surgery for many years, that if it is not the best it is better than the rest.

DR. ALEJANDRO PALOMO (Guatemala City, Guatemala): Since the brilliant presentation of Mr. Millin and Dr. Bacon last year in Buffalo on retropubic prostatectomy, I believe almost everyone has wanted to try the procedure, including myself.

From my personal experience of 27 cases, in which this surgical technique was used, we consider this operation a good one and not a difficult one. In our series of 27 consecutive retropubic prostatectomies, we had only 2 complications; one was a persistent urinary fistula, which required further surgery, and the other one was an abscess in the space of Retzius, which was properly treated.

Dr. Louis M. Orr showed Tuesday afternoon, in his beautiful picture, that it is not necessary to use any special instruments to perform the operation.

In this convention I have seen several modifications of the original technique. We, in Guatemala, follow Mr. Millin's, but, because for some as yet unknown reason, our countrymen do not bleed easily, we just plicate the prostatic capsule, and that takes care of hemostasis.

In conclusion, we do believe that retropubic prostatectomy is an excellent operation, but we also believe that transurethral, suprapubic, and perineal methods are excellent, too.

DR. SAMUEL K. BACON (Hollywood, Calif.): I must say that this subject has activated a considerable amount of enthusiastic discussion. May I summarize by saying it is my opinion that the urologic surgeon must proceed cautiously when utilizing principles of the retropubic approach. As a preliminary consideration and before actual clinical application of the operation, investigation of the space of Retzius is suggested.

The most useful purpose of retropubic prostatectomy is for complete excision of large or medium hyperplasias. This operation has the advantage of affording increased comfort during convalescence, prompt urinary control, and preservation of sexual potency. This is only a transient reference to Dr. Creevy's question in regard to the comfort in the postoperative convalescence in contradistinction to a suprapubic prostatectomy. One hundred and two cases of prostatectomy, with the retropubic approach are reported. The pertinent clinical details and steps of technic significant in obtaining surgical proficiency are described.

Even though only limited experience has been gathered up to the present time, it is my considered opinion that retropubic prostatectomy is anatomically sound, not overly difficult to perform, and that it constitutes a rational procedure for the relief of prostatic obstruction.

I wish to express my sincere appreciation to each one of you, and to my distinguished colleagues, Mr. Terence Millin, Drs. Creevy, Thompson, Grant, and Palomo.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

OSTEITIS PUBIS: ITS DIAGNOSIS AND TREATMENT[1]

LAWRENCE L. LAVALLE AND FRANK C. HAMM
From the Urological Service, the Brooklyn Hospital, Brooklyn, New York

Osteitis pubis is an inflammatory disease of the pubic bone beginning in the symphysis and rapidly involving the pubic rami and even the ischia. It characteristically follows suprapubic incision for prostatectomy or other urinary bladder procedures in a small number of cases. The disease is a distinct entity and follows a definite course. While the disease is self-limiting under expectant treatment, a period of prolonged pain and disability (3 to 12 months) has been the rule in a study of the first 25 reported cases in the literature. Seven cases, have been studied at the Brooklyn Hospital and form the basis for this review. A new therapeutic regime, as instituted in our hospital, has produced rapid amelioration in a matter of days instead of months and will be described in detail.

The condition was first described by Edwin Beer in 1924 and again in 1928. P. W. Aschner in September 1924, Goldstein and Abeshouse in 1929, Peirson in 1929, Kretschmer in 1930, Barnes in 1933, Lazarus in 1936, Wilenski in 1938, Goldstein and Ferber in 1938, Silver in 1941, Wheeler in 1941, Kleinberg in 1942, and Muschat in 1945, have all reported instances of osteitis pubis. Maurice Muschat was able to discover 25 cases, including 2 of his own, in a comprehensive study of the literature. In 1946, H. H. Cohen reported a case and in 1947 E. Kirz, in England, reported 10 cases. Powell's case and the 4 cases of Goldstein and Rubin, makes a total of 41. We are convinced that the incidence of osteitis pubis is much greater than has been reported in the literature as we have information from other urologists of individual instances of this complication in their practices.

CLINICAL DIAGNOSIS

Undoubtedly many mild cases of osteitis pubis have gone undiagnosed in the past. When this disease is better understood and when the urologist maintains a high index of suspicion, more cases will be recognized and treated in an earlier stage. In the typical instance, the patient has had a suprapubic prostatectomy from 3 to 7 weeks before the onset of symptoms. He is at home, walking about, his urinary habits returning to normal and, he may even have returned to his previous occupation. The suprapubic wound and sinus are firmly healed and the urine is now clear, or nearly clear. Without prodromal symptoms he is suddenly seized with pain over the symphysis pubis. In a matter of a few days the pain becomes excruciating and involves one or both pubic rami. The patient experiences great difficulty in locomotion, movement of the lower extremities produces pain along the inner surface of the thighs accompanied by spasmodic contractions of the adductor magnus muscles. Any movement of the trunk or thighs starts a tetanic contraction which cannot be controlled but which subsides in a minute or so if the patient lies or stands quietly. Getting in or out of bed becomes all but impossible due to the deliberate splinting of the recti and adductor muscles to minimize the pain. He lies in bed flat on his back as turning to one side or the other is apt to bring on a new adductor spasm.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

On examination it is immediately evident from the facial expression that severe pain, or fear of pain, is present. He walks to the examining table with short deliberate steps or with a hesitating shuffling gait. He may walk on the tips of his feet in order to spare himself pain transmitted from the heels. He gets on the examining table in slow motion aiming to splint his abdomen and thighs on the pelvic girdle. An attempt by the examiner to spread the thighs is immediately resisted as a painful spasm of the adductor muscles is produced. The slightest pressure over the pubic spine, such as would be normal in the course of an examination, produces exquisite pain. In bed, lying quietly, the pain is bearable. Upon turning or raising his hips for a bed pan, severe spasm returns. Stretching or straining of the recti muscles as he tries to sit up causes pain in the pubic region. If the process extends down to the ischial rami he finds sitting in bed painful. At this point the patient refuses to get out of bed as the effort produces more pain than he is willing to stand. No swelling or redness is noted in the pubic region. A low-grade febrile reaction is generally present. Associated with this is a moderate leucocytosis, polycytosis and secondary anemia as shown in the chart. Microscopic examination of the urine will reveal a few leucocytes. The longer the interval between the prostatic enucleation and the onset of symptoms, the fewer will be the number of pus cells seen in the urine.

ETIOLOGY AND PATHOLOGY

The cause of this unexpected complication in the 7 cases reported here is obscure. They occurred following suprapubic cystotomy. None of the general surgeons or gynecologists at The Brooklyn Hospital recorded a symptom complex suggesting osteitis pubis following their numerous suprapubic midline incisions. There were 4 different operators in the 6 cases so no one technique for suprapubic cystotomy can be culpable. These cases were definitely not space of Retzius infections. The soft rubber drain to the space of Retzius is removed in 24 to 48 hours on our urological service. Pressure of the suprapubic mushroom catheter on the symphysis has no relationship as we do only high suprapubic cystotomies. No heavy retractors are used to separate the recti muscles as no difficulty is encountered in doing a cystotomy on a previously distended urinary bladder. Each of these cases had an uneventful hospital course. None had unusual postoperative hemorrhage or faulty catheter drainage. Urinary sepsis seemed to pay no part in causing this complication.

No biopsies were done on any of these patients so nothing can be added to the scanty knowledge of the pathology of osteitis pubis. Kleinberg gives the best description. Periostitis of the pubic bone is the earliest change. In a later stage partial or complete destruction of the cartilage of the symphysis may occur with separation of the pubic bones. The changes in the pubic rami are the result of destruction and absorption of bone tissue. Later, with healing, bony tissue replacement occurs. This may go too far and periosteal bone formation can result in spurs and complete ossification of the symphysis with fusing of the pubic bones in 12 to 24 months.

ROENTGEN FINDINGS

No roentgen changes were noted in the earliest stage of this disease. In this series clinical signs appeared in 3 to 7 weeks. X-ray corroboration of osteitis pubis was not noted until 4 to 13 weeks after the second-stage operation. In an individual case, x-ray confirmation is not found until 1 to 9 weeks after the onset of symptoms. Hence, repeated studies at weekly intervals are necessary to elicit the earliest roentgen changes to confirm the diagnosis. At first, a fuzziness or fraying of the periosteum of the symphysis or pubic ramus is seen. Within 2 more weeks the moth-eaten appearance of bone destruction in the pubic ramus is manifested. The appearance is not unlike the lytic process seen with metastases from a prostatic carcinoma or from some inflammatory involvement of the bone. Complete bony repair may occur as in case 4, or spur formation, ossification of the symphysis or dense calcification to the bone occur as in case 2. As it may take 1 to 9 weeks after the onset of symptoms to obtain positive x-ray findings, treatment should be instituted on the basis of a clinical diagnosis to spare the patient pain, disability, and a prolonged hospital stay.

TREATMENT

In cases 1 and 2 sulfonamides and penicillin were administered for 2 weeks without changing the clinical course in the slightest. On the presumption that we were dealing with a trophic disease such as a polyneuritis, high vitamin B administration was considered. It was felt that diathermy, although condemned in some previous papers, might be beneficial. Hence a vitamin B complex preparation[2] was administered intramuscularly twice a day along with daily short-wave diathermy to the affected parts. Improvement occurred within a matter of days and the first 2 patients were so promptly relieved of their pain that we determined to use it in future cases. In case 3, high vitamin B complex administration by mouth and short-wave diathermy were instituted promptly, without previous use of chemotherapeutic agents. Improvement was noted on the third day. Case 5 was treated as an office patient, daily injections of Solu-B plus a high potency vitamin capsule[3] by mouth was rewarded by prompt improvement without short-wave diathermy. Case 6 responded to this therapeutic regime in 6 days. Expectant therapy for osteitis pubis as studied in the literature revealed that amelioration would occur in from 3 to 9 months or more. In short, the treatment of this painful complication consists of the intramuscular or intravenous administration of Solu-B, oral administration of high potency B complex capsules and daily short-wave diathermy to the affected areas. Therapy should commence as soon as clinical symptoms appear and weekly roentgenograms of the pelvic girdle should be obtained for confirmation of the diagnosis of osteitis pubis.

---

[2] Solu B, Upjohn.

[3] Zymacap

A recent patient following retropubic prostatectomy did not show the expected response to B complex and Dr. John Pepe, our roentgenologist, advised a trial of roentgen therapy. A good effect was obtained. Goldstein and Rubin treated 4 cases of osteitis pubis with roentgen therapy and they noted a good response. It is our opinion that high dosage of B complex should be tried in all cases of this complication and that the refractory case should receive deep x-ray therapy. There should be little objection to using both modalities in a severe case.

No opportunity to use streptomycin has presented itself. This is worth doing in the light of a recent observation that osteitis pubis may be a low-grade chronic infection due to B. proteus. (Reported by Powell.)

CASE REPORTS

Case 1. D. H., aged 72, underwent a 2-stage suprapubic prostatectomy, the gland being enucleated on March 22, 1946. He left the hospital in 2 weeks with a firmly healed suprapubic wound. He returned to the hospital 3 weeks later with the history of increasing inability to walk, and pain over the left pubic bone. He was put on 30,000 units of penicillin every 3 hours and sulfathiazole, 2 gm. daily, for a period of 2 weeks. The symptoms increased in severity requiring morphine for pain. He remained in bed presenting an abject picture. Intramuscular injections of Solu-B and short-wave diathermy was started on May 12, 1946, and within 2 days he experienced rapid improvement and was able to walk around his bed and to the bathroom. No evidence of osteitis pubis was noted on the admission study, the x-rays not becoming positive until 8 weeks following the second stage. See figure 1.

FIG. 1. Case 1. *A*, Eight weeks after prostatectomy we first notice decalcification at symphysis. *B*, Progression of disease continues. Note increase in decalcification and widening of symphysis. *C*, Calcium deposition is noted with marked separation of symphysis, 5 months after prostatectomy.

Case 2. A. W., aged 68, underwent a 2-stage prostatectomy, the second stage being performed on February 15, 1946. He was discharged from the hospital in 2 weeks with a firmly healed suprapubic wound. One week after his discharge from the hospital he noted increasing pain over the symphysis which radiated down both thighs and caused severe pain when he tried to walk. On re-admission he was given penicillin and sulfathiazole for 4 weeks without improvement. Intramuscular B complex and diathermy were instituted on May 12, 1946, and in 2 days the patient was able to get out of bed without help, was free of pain, and able to take longer steps. His roentgenogram findings became positive for osteitis pubis 4 weeks after the second-stage prostatectomy. Roentgenograms taken

7 months later, in January 1947, revealed calcification of the widened cartilage of the symphysis pubis and some spur formation in both pubic rami. See figure 2.

Case 3. E. R., aged 57, underwent a 2 stage prostatectomy, the second stage being done on August 27, 1946. He was discharged with a healed suprapubic wound 10 days later. He was comfortable for nearly 3 weeks when he began to notice pain at the suprapubic area radiating down both thighs. He was able to walk with great difficulty until the pain and adductor spasm became so great that he returned to the hospital on October 14, 1946. Upon admission a clinical diagnosis of osteitis pubis was made based on the experience gained from cases 1 and 2. No chemotherapy was used. He was placed on high B complex medication and given daily short-wave diathermy. In 3 days marked improvement occurred. He was able to walk about his room and in a week he left the hospital. Roentgenograms taken 4 months later, in February 1947, revealed no evidence that would indicate osteitis pubis. It is believed that early diagnosis and prompt treatment aborted further progress of this disease and rapid resolution of the bone disease. See figure 3.

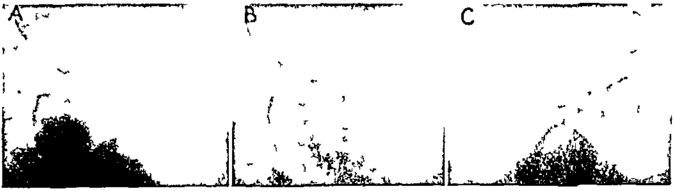


FIG. 2. Case 2. *A*, Thirteen weeks after enucleation and 9 weeks after onset of symptoms we note decalcification and separation at symphysis. *B*, One month later we note beginning redeposition of calcium. Separation of symphysis is marked. *C*, Eleven months after prostatectomy we can see maximal redeposition of calcium with lessening of symphysial separation.

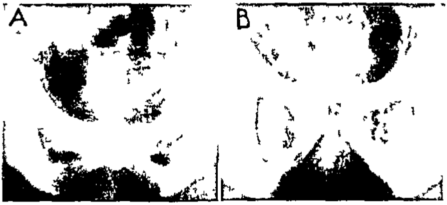


FIG. 3. Case 3. *A*, Film taken 7 weeks after prostatic enucleation. Note decalcification of both pubic rami. *B*, Film taken 6 months after prostatectomy. Note good healing with redeposition of calcium and moderate separation at symphysis.

Case 4. F. S., aged 71, underwent a 2-stage prostatectomy, the enucleation being performed on December 10, 1946. He left the hospital 2 weeks later with a dry suprapubic wound. For 6 weeks the patient felt perfectly well, had good control of urination, and had no nocturia or frequency. Without warning he began to experience pain and tenderness over the right pubic area. A local physician prescribed codeine and aspirin with some measure of relief. Bending, turning and walking caused pain in his right thigh and he was forced to use a cane for walking. On examination in the office no local signs of inflammation in the wound, right pubic area, or right thigh were found. Adductor spasm was marked. A clinical diagnosis of early osteitis pubis was made on February 17, 1947, and daily injections of Solu-B were instituted. The patient also took 3 Zymacap capsules daily. No diathermy was used. In 6 days amelioration occurred and the patient was able to forego the use of his cane. He was spared an additional hospital admission by prompt clinical diagnosis and office treatment.

Case 5. H. P., was aged 65. On August 29, 1944, a V shaped piece of tissue was resected from the bladder neck through a suprapubic incision. He was admitted to the hospital 4 weeks later with osteitis pubis. The diagnosis of osteitis pubis was made in retrospect. The clinical chart revealed that many consultations were made to determine the cause of his pain and bilateral adductor spasm. A neurologist, an orthopedist, and an internist all failed to diagnose his disease. He was treated with bed rest, codeine and aspirin and also with occasional hypodermic injections of morphine when his pain was severe. The x-ray findings of osteitis pubis were completely missed at that time and a roentgen diagnosis was made 3 years later when the films were reviewed in the light of our new experience. He left the hospital after 3 months, using a cane, and being far from well. He was not free of adductor spasm and pain over the pubic rami, for 9 months, but he has been completely well for the past 3 years. This patient closely followed the pattern of prolonged disability in those reported cases which had received expectant treatment.

Case 6. P. F., aged 71, had a 1-stage prostatectomy performed on February 21, 1947. He left the hospital on the twenty-third postoperative day with a healed suprapubic wound and good urinary control. Two weeks after leaving the hospital he was seen in the Out-Patient Department with the complaint of pain over the pubic bone with radiation to the inner upper aspect of both thighs. Within 1 more week the pain increased in severity. He had great difficulty in walking, getting on and off the examining table and had a temperature of 101 F. He was hospitalized and 100,000 units of penicillin every 2 hours for 3 days was then tried without subjective relief. Motion pictures of the patient demonstrating his marked disability were taken on April 11, 1947. Intramuscular injections of Solu-B 3 times a day and short-wave diathermy daily were instituted on the following day. In 6 days his pain was greatly diminished, he was able to get in and out of bed, and he was able to walk to and from the bathroom with steps of 14 to 16 inches in length. The x-rays became positive on April 21, 1947, or 3 weeks after the onset of symptoms. Films taken 7 months later showed marked redeposition of calcium at the symphysis and the formation of many bony spurs on the descending rami of the pubes. See figure 4

DISCUSSION

The diagnosis of osteitis pubis can be readily made on the clinical signs and symptoms. The x-ray confirmation completes the diagnosis but such confirmation is not obtained until 3 to 7 weeks after the clinical diagnosis has been made. Treatment of this painful complication should not be postponed until x-ray evidence is obtained A roentgenogram of the pelvic girdle at weekly intervals is recommended Mild cases of osteitis pubis occur and not all cases are crippled and confined to bed

Why this obscure complication occurs is difficult to say. Careful study of the clinical charts reveals no unusual operative or postoperative findings. All of these cases had the average post-prostatectomy hospital course without superimposed infection or secondary hemorrhage. No bacteriological studies were made since no localized exudates were discovered. The secondary anemia noted in all of these cases may have some etiological significance. Yet numerous men in their sixth to eighth decade present a similar mild secondary anemia.

Early recognition of this complication in the postoperative office consultation will enable the physician to assure the apprehensive patient that no serious consequences will ensue and that response to treatment will be prompt. He can be assured that no other organs or structures will be involved. The patient can also be told that there will be no need for hospitalization as treatments can be carried out in the office. This assurance will spare the patient a great deal of apprehension.

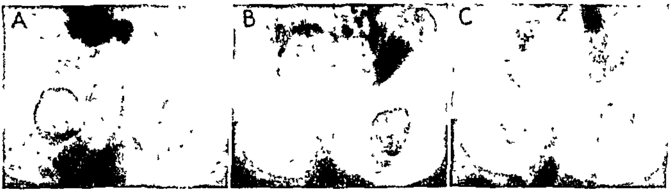


FIG. 4. Case 6. *A*, Four weeks after onset of symptoms we note first roentgen changes at symphysis. *B*, Note widespread bone destruction about 4 months after enucleation. Spread of disease towards ischial spine may be seen. *C*, Seven months after enucleation we note redeposition of calcium Many bony spurs now seen on descending rami of pubes.

We feel that as the retropubic approach for prostatectomy becomes more popular the incidence of osteitis pubis will increase. This should not act as a deterrent to performing this valuable operation. Should osteitis pubis occur in a small percentage of cases, the diagnosis can be made early and treatment with the B complex as outlined, or the deep x-ray therapy, as done by Goldstein and Rubin, may be administered promptly.

CONCLUSIONS

Seven cases of osteitis pubis following suprapubic prostatectomy are presented.

Early diagnosis can be made on the basis of clinical signs alone.

Although the disease is self-limiting with improvement in 3 to 9 months, a new therapeutic regime to hasten recovery is presented. When this fails recourse to deep x-ray therapy should be tried.

The importance of repeated roentgen examination to reveal bone disease is stressed.

Credit to Edwin Beer and Paul Aschner is given for the original description of this disease.

80 Hanson Place, Brooklyn, N. Y.

REFERENCES

Aschner, P.: J. Urol., **12:** 259, 1924.
Barnes, F. L.: Texas State J. Med., **28:** 601, 1933.
Beer, E.: Int. J. Med. & Surg., **37:** 224, 1924.
——: J. Urol., **20:** 233, 1928.
Cohen, H. H.: J. Urol., **55:** 84, 1946.
Goldstein, A. E. and Abeshouse, B. S.: Surg., Gynec. & Obst., **49:** 477, 1929.
—— and Ferber, W. L. F.: J. Mt. Sinai Hosp., **4:** 1052, 1938.
—— and Rubin, S. W.: Am. J. Surg., **74:** 480, 1947.
Kirz, E.: Brit. J. Surg., **34:** 272, 1947.
Kleinberg, S.: J. Urol., **48:** 635, 1942.
Kretschmer, H. L. and Sights, W. P.: J. Urol., **23:** 573, 1930.
Lazarus, J. A.: Ann. Surg., **103:** 310, 1936.
Muschat, M.: J. Urol., **54:** 447, 1945.
Peirson, E. L.: Surg., Gynec. & Obst., **49:** 834, 1929.
Powell, N. B.: J. Bone and Joint Surg., **29:** 785, 1947.
Silver, C. M.: Bull. of Hosp. f. Joint Dis., **2:** 10, 1941.
Wheeler, W. K.: J. Urol., **45:** 467, 1941.
Wilensky, A. C.: Arch. Surg., **37:** 371, 1938.

THE JOURNAL OF UROLOGY
Vol 61, No. 1, January 1949
Printed in U.S.A.

DISCUSSION

DR. LOUIS M. ORR (Orlando, Fla.): While I have enjoyed very much this discussion of osteitis pubis, I must confess that in my not too few years of dealing with conditions requiring opening of the urinary bladder, I have never recognized or seen this postoperative complication.

The addition of 6 cases of this condition all from one locality to a sum total of only 25 which the authors found in the literature would seem to indicate that either the disease is somewhat difficult of recognition or that there has been negligence on the part of many in recording their observations. If Noel Coward had been asked to take part in this discussion he would doubtless say that "anything might be expected from Brooklyn."

Despite the paucity of case records in the literature of osteitis pubis, recent personal communications record the fact that since retropubic prostatectomy has been on trial in this country, several cases of osteitis pubis have been reported following this particular procedure.

From the description and clinical course of the disease as given by different reporters, it would seem that the condition is distinctly self-limiting and would seem to be first periostitis and, secondly, true osteitis without involvement of the marrow and furthermore without the presence of any suppuration. After healing has taken place a certain degree of ossification of the pubic cartilage with generalized thickening of the periosteum has been noted.

This entire clinical picture suggests quite strongly that trauma, in some form, associated with interference to the nutrition of the periosteum be it from the pressure of the hand against the pubis, which sometimes reaches the point of violence in enucleating a difficult prostate, or the pressure of a retractor, in the hands of a spirited assistant might be sufficient to induce periosteitis. The delay in appearance of symptoms could be accounted for on this basis.

It is to be noted that all cases here reported have followed suprapubic enucleation of the prostate. The authors are to be congratulated upon the effects of their scheme of therapy and the rapid response to the administration of vitamins is highly suggestive of a deficiency aspect of the disease.

I feel that we will all be much the wiser from hearing this interesting presentation and no doubt our diagnostic acumen will be considerably sharpened and we will be more alert in the future for this distressing complication.

DR. H. W. BRUSKEWITZ (Madison, Wis.): I have enjoyed the paper by Doctors Lavalle and Hamm. Their plan of active treatment will, I am sure, afford the patients with this most distressing complication, more rapid relief.

Within a year we have observed three instances of this complication; we have never observed one previously. The occurrence of the first of 3 three cases prompted my associate, Dr. George H. Ewell, and myself to present a discussion of the subject before the North Central Section in October 1947.

Certainly, one could hardly fail to overlook this complication since the patient is totally incapacitated, and the psychic trauma is quite marked.

Having observed with our colleagues cases of Sudeck's atrophy in the long bones following trauma, and because of the clinical course, x-ray findings and other reasons, we are inclined to agree with Wheeler that the condition is acute bone atrophy. Residual symptoms may persist for months or years.

We know, through personal communication, of 2 cases that followed transurethral resection and 1 case in a woman following ureterolithotomy (pelvic ureter).

In our hands, except for the use of one piece of Oxycel gauze over the bag of the Wolf or Foley catheter, the use of smaller catheters, smaller and earlier removal of the suprapubic tube which has resulted in more rapid closure of the wounds, there has been no essential change in the technique of the operation. The bladder is routinely sutured to the anterior abdominal wall during the enucleation.

F. S., aged 60, approximately 7 weeks following a 1-stage suprapubic prostatectomy, exhibited the typical symptoms of osteoporosis. The postoperative recovery was uneventful other than that the suprapubic sinus was slower than usual in closing. A cystogram (slide) shows normal pelvic bones prior to operation. The typical bone changes at the time of admission, 8 weeks following operation, are shown in this slide (slide). The next slide shows the marked changes 12 weeks following the onset of symptoms. The next slide shows ossification of the symphysis and residual bone changes 1 year following the onset. The patient still presents symptoms. He was treated expectantly with a high caloric diet, tonics, analgesics, vitamin B elixir by os and by hypodermic.

G. R., aged 57, was admitted on July 7, 1947 because of hemorrhage from a peptic ulcer. He received 12 transfusions and had bilateral superficial femoral vein ligations because of thrombophlebitis with pulmonary infarcts. Urinary retention developed, and examination disclosed grade 2 benign prostatic hypertrophy. He was unable to void following several days of Foley catheter drainage. Since his general condition was such that prolonged drainage would be required, on August 4, 1947 a suprapubic cystotomy was done. On October 31, 1947 a second stage suprapubic prostatectomy was performed. The postoperative recovery was uneventful and he was discharged on November 10, 1947, voiding well, with no residual urine and the wound healed. On the day of discharge he complained of vague pains in and about the left groin and left thight. These were assumed to be secondary to the thrombophlebitis.

He was readmitted on December 5, 1947 with the typical history and physical findings of osteoporosis. (Slide) Six weeks postoperative, no remarkable changes, although the clinical history and physical findings are diagnostic. (Slide) Seven weeks postoperative, again no remarkable changes yet in retrospect definitely diagnostic. (Slide) Nine weeks postoperative, typical changes of osteoporosis. He was given vitamin B complex per os and by hypodermic, a high caloric diet and a course of deep x-ray therapy. Progress was slow and he developed a marked psychosis. He was discharged on March 9, 1948, approximately 3 months after being readmitted.

E. C. S., aged 63, had a 1-stage suprapubic prostatectomy on March 19, 1948.

The prevesical space was exposed for a retropubic operation. A very large vein was injured, the bleeding was controlled by a tampon of a small piece of Oxycel gauze. The bladder was opened and a prostate weighing 70 gm. was enucleated. A Wolf catheter covered with one piece of Oxycel gauze and inflated with 30 cc water was left in place, and also a 26 F. suprapubic tube. The Wolf bag was gradually deflated and removed in 48 hours, and the suprapubic tube in 72 hours. A 20 Foley catheter was inserted. The postoperative course was uneventful, except for a seropurulent sanguinous discharge that persisted for several days after urine drainage had ceased, and a low grade febrile reaction. He was discharged (April 10) twenty-two days following operation. His first symptoms of pain in the right groin and suprapubic region and pain on motion of the legs were noticed 25 days following the operation. (Slide) X-ray examination (April 17) four weeks postoperative. Without experience this film made at this early date could be confusing. (Slide) This film 7 weeks postoperative shows unmistakable 'evidence of the disease. This patient has received diathermy and x-ray therapy and vitamin B. His immediate progress has been much faster than the two former cases.

From our observations of this case and the preceeding one, we are impressed with the fact that clinical symptoms are present in some cases several weeks before x-ray changes are demonstrable. We should not wait for, nor rely on x-ray evidence alone. The diagnosis can be made clinically early and treatment instituted early.

Dr. Thomas D. Moore (Memphis, Tenn.): If, as has been suggested, the occurrence of osteitis pubis is on a geographic basis we have had a mild epidemic in the vicinity of Memphis. I might state that through the years in the almost routine performance of primary suprapubic prostatectomy for glands of unusually large size and transurethral resection of those of lesser degree, we have never recognized a single instance of osteitis pubis. During the past year, however, this distressing complication has occurred in 8 cases of approximately 65 primary extravesical retropubic prostatectomies, the performance of which followed closely the technique of our distinguished honorary member, Mr. Terence Millin. We have been meticulously careful in aseptic technique, in obtaining a water-tight closure of the prostatic capsule and in the avoidance of trauma by tractors or by pricking of the periosteum with a needle. More recently we have incised transversely the endopelvic fascia at the level of the symphysis in an attempt to conserve a protective covering of tissue posterior to the symphysis as an added precaution.

Primary healing of the incision occurred in practically all of the 65 cases and in those which developed osteitis pubis there was no external evidence of an inflammatory process, such as redness or swelling, and in the early stages there was no roentgen evidence of osseous changes. The earliest onset of symptoms was 2 weeks after the operation, the latest was 5 months postoperatively and the average time of onset for the group was 2 months. These patients were severely disabled; they lay in bed immobile, carefully avoiding any motion of the pelvis or hips because of the constant dread of precipitating a terrific paroxysm of pain involving the adductor magnus group of muscles on the inner aspect of the thighs. They were re-admitted to the hospital and films exposed from time to time later displayed changes involving the periosteum and slight widening of the symphysis. None required surgical interference. The duration of symptoms was comparatively brief after instituting treatment consisting of the free use of the antibiotics, combined with local heat and massive doses of vitamin B-1. Most of the patients were able to be up and about fairly comfortably within a week or ten days.

We should be greatly indebted to Drs. Lavalle and Hamm for this most timely and interesting presentation and their valuable suggestions regarding the management of this disturbing complication.

DR. DAVID B. STEARNS (Boston, Mass.): I wish to compliment Dr. Lavalle and Dr. Hamm for bringing up this important subject. From the talk you can hear in the corridors, I believe that there are more cases throughout the country of osteitis pubis than are reported.

I visited my house service Tuesday and found a fresh case of osteitis pubis which came from a Burlington, Vermont hospital following a 2-stage prostatectomy.

At the Beth Israel Hospital we have had a case following retropubic prostatectomy. A man 60 years old, in excellent condition, worked in the out-patient department, was admitted to the hospital on November 3, 1947. He was operated on November 6; and his highest temperature following operation was 99.6 F. The drain was removed in 48 hours, the catheter in 6 days, and he was discharged on November 16 with a dry wound, perfectly well.

He was seen twice in the out-patient department within 2 weeks, and he was voiding well; the wound was dry; he felt fine, and the urine was clear. Thirty-eight days after operation he noticed the first slight pain in the region of the symphysis, and then on December 27 appeared in the out-patient department, barely able to walk. He was re-admitted and the diagnosis of osteitis pubis was made: white count 15,000, nonprotein nitrogen 34, temperature 99 F., urine culture positive for B. coli. He was put to bed and given antibiotics; was given heat and strapped, but the condition did not seem to improve rapidly. He improved slowly with heat and opiates; these were the best remedies in his case. He was discharged 53 days after readmission. (Slide) This first slide shows the patient before operation. Urogram was done, showing enlarged prostate. Notice prostatic hypertrophy and hooking of ureter. Symphysis pubis smooth and regular. Bony structure normal. (Slide) This shows symphysis on December 29. Notice irregularity and erosion of inner margin. (Slide) This shows the patient on January 13. There is progression and irregularity, and erosion downward on the inner margins of the symphysis. Note widening of symphysis pubis. (Slide) This was taken February 15. Here there is marked widening of the symphysis, essentially the result of loss of bone substance.

It is my opinion that there are more cases of osteitis pubis than we think. Most of us do not bother reporting these cases.

I also want to point out that I doubt whether the case I have reported resulted because of the fact that it was a retropubic operation. It happened to be one of our smoothest cases from an operative point of view, and I doubt very much that it was due to that.

I agree that from our present knowledge the etiology of osteitis pubis has as yet not been established.

DR. LAWRENCE L. LAVELLE (Brooklyn, N. Y.): Including Dr. Goldstein's recent cases and the 10 reported by Dr. Kerrs of England, there are but 41 instances of osteitis pubis in the entire literature. This disease is by no means a rare one. Both Dr. Hamm and I have been approached by at least a dozen surgeons during this meeting all of whom recall one or more cases of osteitis pubis.

I wish to say that only two of these complications were noted in our series of 50 retropubic prostatectomies and this incidence should not cause us to abandon so valuable an approach to the treatment of prostatic hypertrophy. This disease no longer needs to be treated expectantly. It can be attacked by the administration of large doses of B-complex and diathermy, and where unsuccessful, by deep x-ray therapy, as outlined by Dr. Goldstein. The patient can be assured that his condition will improve and that a second hospital admission need not be necessary.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

URINARY INCONTINENCE FOLLOWING PROSTATECTOMY: ITS CURE BY NONOPERATIVE TREATMENT[1]

ALBERT VERGÉS-FLAQUÉ

From the Department of Urology (James Buchanan Brady Foundation) of the New York Hospital, New York, N. Y.

The object of this paper is to present a nonoperative method of treating postoperative urinary incontinence which, although carried out in only a small series of cases to date, has yielded such encouraging results as to make me feel that many others with this distressing handicap may not only be greatly benefited thereby, but, in a considerable percentage of cases, cured.

The first 10 patients treated by this method, and who constitute the present series, were incontinent because of operative procedures carried out upon the prostate gland, both for benign hypertrophy and for carcinoma. Urinary incontinence may follow any type of prostatectomy. Postoperatively, when all drains and packings have been removed, and there is no urinary fistula, the majority of patients have perfect urinary control. There is a small group who suffer temporary incontinence which gradually diminishes until, after several weeks or months, the patient has regained complete urinary control. There is an even smaller group whose incontinence seems to resist all forms of treatment and who must wear rubber urinals, Cunningham clamps, or some self-devised receptacle to collect the urine.

REVIEW OF 10 CASES

Condition present. In all 10 cases reviewed here, the physiology of micturition was considerably disrupted. The internal sphincter was injured to a greater or lesser degree; and endoscopically it was observed that such fibers as remained did not contract voluntarily, nor did they show any ability to stop a flow of water at low pressure. All of the bladders showed good capacity. Endoscopically—except in 1 case—the external sphincter was seen to relax and contract in all its circumference when the patient was instructed to start and stop the stream. It was in this ability of the external sphincter to contract at the volition of the patient that dependence was placed for the success of the treatment.

Incontinence in these cases had existed for periods varying from 1 month to 5½ years. The 2 cases of short duration (1 and 2 months respectively) are included because these patients had shown no improvement whatsoever up to the time they were first seen, and were totally incontinent. All of the 10 patients remained dry at night.

Examination of patient. The patients were carefully studied from the following standpoints: 1) their symptoms previous to prostatectomy, 2) the type of prostatectomy that was done, and the pathological diagnosis, and 3) the duration of postoperative urinary incontinence, the treatment received, and the extent of improvement (if any). Urinalysis, rectal palpation, urethral calibration, cystoscopy and endoscopy, and cystometry were all done. The bladder was filled with fluid and the patient tested as to his ability to start and stop the stream. In 2 cases urethrograms were taken during voluntary contraction and relaxation of the external sphincter.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 20, 1948.

Previous to prostatectomy, most of the patients had the usual diurnal and nocturnal urinary frequency, and residual urine ranging from 80 to 300 cc. Three had acute urinary retention. The prostates were from 1½ to 3 times the normal size.

Six patients had total perineal prostatectomy (removal of the gland and its capsule), 2 had radical perineal prostatectomy (removal of the prostate with its capsule and the seminal vesicles), 1 had simple perineal prostatectomy, and 1 had transurethral resection.

Three of the removed glands were carcinomatous, 1 of these showing invasion of the seminal vesicles; 6 showed benign hypertrophy, and in 1 case (operated upon in another hospital) the pathological diagnosis could not be learned (table 1).

TABLE 1

NO.	AGE	TYPE OF PROSTATECTOMY	PATHOLOGY	DURATION OF INCONTINENCE		DURATION TREATMENT	RESULTS
				yrs.	*mos.*	*mos.*	
1	68	Total perineal	Benign hypertrophy		10	11	Good
2	62	Perineal	Carcinoma		1	1	Cured
3	71	Radical perineal	Carcinoma	2		6	Failure
4	55	Transurethral	Benign	1½		4½	Good
5	60	Total perineal	Benign	4½		6	Cured
6	68	Radical perineal	Carcinoma		10	6	Good
7	66	Total perineal	Unknown	1		3	Cured
8	73	Total perineal	Benign		2	1½	Cured
9	73	Total perineal	Benign	4		7	Cured
10	72	Total perineal	Benign	5½		4	Good

The duration of postoperative urinary incontinence varied from 1 month to 5½ years.

In no case did cystoscopy reveal any lesion which might account for the incontinence.

The bladder capacity in the 10 cases ranged from 300 to 650 cc.

Sounds up to 27 F. were passed with ease in all but 1 case; in this, there was a stricture in the prostatic urethra which would admit nothing larger than a 14 F. instrument.

The most important step of the examination is endoscopy, the vital finding being the ability of the external sphincter to contract and relax. In only 1 case was this ability lacking.

The second most important step is determining the ability of the external sphincter, upon contraction, to stop a flow of fluid going *into* the bladder, against the highest possible pressure as registered in a water manometer.

The method of determining this pressure is illustrated in figure 1. An adjustable glass flask, containing 500 cc of saline solution (fig. 1, *A*), is connected by means of a glass Y connecting-tube and rubber tubing to a catheter whose tip is in the anterior urethra. A water manometer, also on an adjustable stand (fig. 1, *B*), is connected to the other arm of the Y connecting-tube.

A Hyams penile clamp is applied, to prevent the escape of fluid between the catheter and the urethral wall. The patient is told to contract the external sphincter. A flow of saline solution, at very low pressure, is started from the flask, passes through the catheter, and fills the portion of the anterior urethra between the clamp and the external sphincter. When the intraurethral pressure in this segment of the urethra reaches the pressure in the manometer, the flow ceases. The pressure in the water manometer is gradually raised until the external sphincter can no longer resist the pressure of the fluid and relaxes, allowing the solution to enter the bladder. The pressure registered in the water manometer just before the external sphincter relaxes is designated as "maximum sphincteric-contraction pressure."

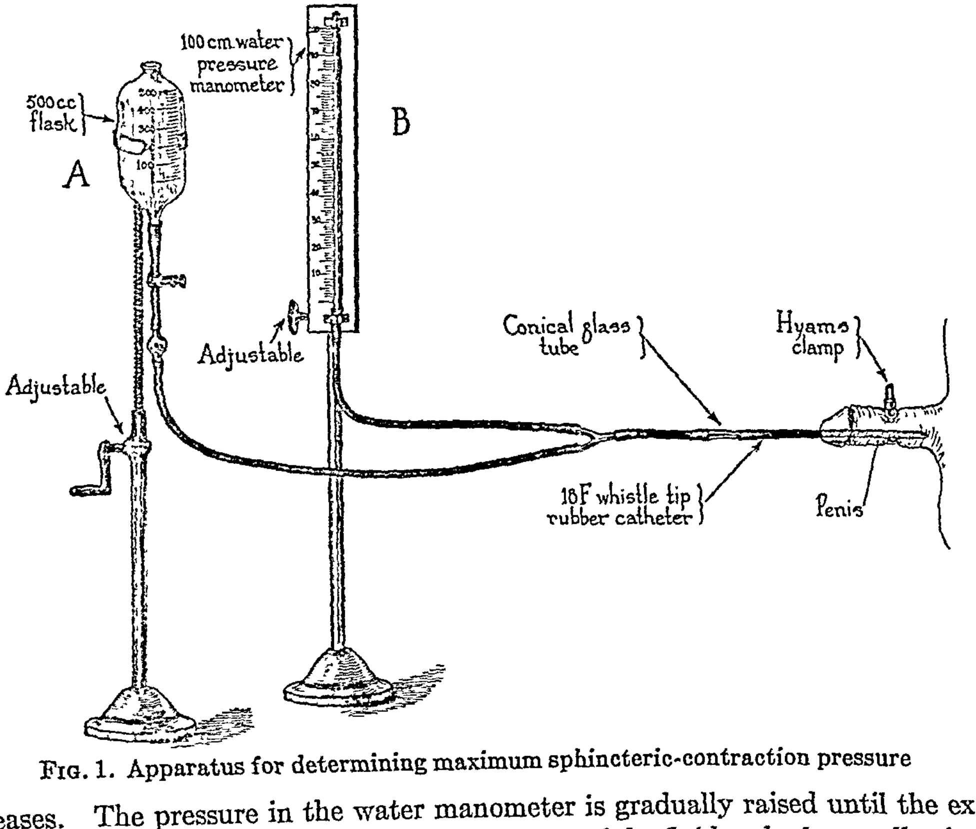


FIG. 1. Apparatus for determining maximum sphincteric-contraction pressure

By cystometric examination it is then determined how much fluid the bladder must contain in order to attain an intravesical pressure of the same level as the maximum sphincteric-contraction pressure, this volume being the maximum amount that the patient can, as a rule, hold and still remain dry.

Treatment. Sounds are not used in this treatment, unless there is present a stricture of less than 20 F. caliber.

It is first carefully explained to the patient that the preliminary studies have shown him to be a satisfactory subject for a course of treatment, but that a successful result will depend largely upon his own willingness and ability to follow instructions and persist with treatment.

The patient's bladder is filled with from 200 to 500 cc of silver nitrate solution, 1:10,000, and he is requested to stand up and start and stop urination about three times. "Stopping urination" means complete cessation of the flow for several seconds. He is then told to walk back and forth a few times, and the exercises are started again. When starting urination, the patient is instructed to contract his abdominal muscles and relax his perineum; when attempting to stop the stream, he is instructed to relax his abdominal muscles and contract his perineal muscles. These instructions must be explicit, as it is of the greatest importance that the patient understand what is expected of him. Frequently he must be told to tighten the rectum, or the buttocks, so as to produce contraction of the external sphincter. As treatment progresses, he is told to flex the thighs and knees, cough, and separate the legs, while holding his water. The patients always show very poor ability to retain their water in the first few treatments, but gradually they improve. They receive treatment twice a week, at least.

The patient is told to do these exercises upon arising in the morning, the bladder then being fairly full. When there is definite improvement—that is, when the patient is able to hold his urine while walking—then comes the crucial moment to tell him to discard the clamp or rubber urinal. This he will not do, unless he can be convinced that he can do it. We fill the bladder with 150 cc of solution, adjust a pad in front of the penis, and instruct the patient to walk for 2 hours with sitting intervals. The clamp or urinal is kept in the clinic. The first few times he returns quite wet, but as time goes by, he is encouraged as he sees that he can keep dry for 2 hours or more, voiding not less than 200 cc. True, at the end of the day, when he is tired, his ability to hold his water is less; but this, too, is gradually overcome.

Passing sounds (unless there is a stricture of less than 20 F. caliber), irrigating the bladder, and telling the patient to start and stop the stream a few times in the clinic, and then sending him home with instructions to practice the latter each time he urinates, is not, in this author's opinion, the proper approach to the problem of postoperative urinary incontinence in the male. Most surgical operations for the relief of this condition have as their aim the narrowing or constriction of the urethral lumen in the sphincteric region. The passage of sounds, on the other hand, dilates the lumen. If the object of passing sounds is the passive exercise of the urethral sphincter, then it would seem that active exercise, by voluntary contraction, is preferable.

Results of treatment. The results of treatment in these 10 cases were as follows: cured, 5; good, 4; failure, 1 (table 2).

The 5 patients discharged as "cured" were able to dispense with clamps or rubber urinals, and during the day, pursuing their regular activities, retained their urine perfectly for periods of from 3 to 5 hours.

The 4 patients whose results were regarded as "good" were able to keep dry during the day for from 2 to 4 hours, except under conditions of special stress, when they sometimes lost a few drops of urine. Unlike the ordinary case of so-called "stress incontinence," however, this did not occur upon coughing or sneezing, but only under conditions of physical activity requiring vigorous contraction of the abdominal muscles. For example: one patient, a coal miner, with a fat abdomen, usually lost a few drops of urine when bending over to raise a heavy object in the course of his occupation.

The one failure in this series was a 71 year old man who had had a radical prostatectomy for carcinoma involving the seminal vesicles, and had been incontinent for 2 years. No sphincteric contraction was observed endoscopically, and, upon being tested, the sphincteric-contraction pressure was found to be zero. Although treated for a period of 6 months, there was no improvement whatsoever in this case, indicating that the external sphincter was destroyed or functionless.

TABLE 2

NO.	SPHINCTERIC CONTRACTION ENDOSCOPIC	MAXIMUM SPHINCTERIC-CONTRACTION PRESSURE—WATER	RESULTS OF TREATMENT		
			Stayed dry	Urine voided	RESULTS
		cm.	*hours*	*cc.*	
1	Good*	35	3	300	Good
2	Good	40	4	300	Cured
3	Absent	0	Always wet	0	Failure
4	Good	45	4	280	Good
5	Good	40	3	350	Cured
6	Good	25	2	200	Good
7	Good	36	3	300	Cured
8	Good	38	4	250	Cured
9	Good	40	5	300	Cured
10	Good	36	2	250	Good

* In entire circumference.

SUMMARY

A nonoperative method of treatment of postoperative urinary incontinence, consisting of exercises to develop to its maximal capacity the contractile ability of the external sphincter, is described.

Ten cases of postoperative incontinence treated by this method are reviewed. The patients ranged in age from 55 to 73 years. All had had some form of prostatectomy for either benign hypertrophy or carcinoma.

Two patients had been incontinent for 1 and 2 months respectively; the remainder from 10 months to 5½ years. All remained dry at night, indicating that ability of a patient to keep dry during sleep does not necessarily mean that he has good urinary control.

The duration of treatment in these 10 cases ranged from 1 to 11 months.

Five patients were cured (that is, were able to dispense with clamps or rubber urinals, and retained their urine for from 3 to 5 hours during the day). Four had good results (that is, remained dry for from 2 to 4 hours, except under conditions of special stress, when they sometimes lost a few drops of urine). In 1 case there was no improvement whatsoever.

CONCLUSIONS

From our experience with this method of treatment to date, it is concluded:

That certain cases of incontinence of urine following prostatectomy are curable if treated by properly performed exercises to develop the contractile ability of the external sphincter. This method of treatment is not, of course, indicated in cases with destruction of both the external and internal sphincters.

That, as a rule, the earlier these exercises are started, the shorter will be the duration of treatment.

That frequent and prolonged contact with the patient is essential in the treatment of postoperative urinary incontinence.

I wish to thank Dr. Oswald S. Lowsley for his helpful suggestions and for placing the facilities of his Department at my disposal; and Mr. William P. Didusch for his splendid illustration which so admirably depicts the method of examination described here.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

DISCUSSION

DR. JOHN DOUGHERTY (Knoxville, Tenn.): Urinary incontinence following operations in the region of the bladder neck on male patients is a constant and provoking source of worry to the operator. There are none of us here who have not had our possibly high evaluation of our surgical ability completely deflated by the individual who returns to the office for his first visit after his operation, and tells us in evasive terms that he is doubtful if his operation did him any good, since he cannot hold his water. At this stage in the game he has forgotten how difficult it may have been and what pain he experienced trying to pass even a small drop or two prior to his operation, but now the constantly running stream makes him desirous of something to control it.

Dr. Vergés-Flaqué has presented us with a unique method of improving on this very real problem, and in his series of cases it has certainly worked advantageously. I gather from reading his article that the principal conclusion is that the reason for the poor control following prostatic surgery, and particularly perineal surgery, has been a failure, either permanent or temporary, for resumption of satisfactory control by the external sphincter. His idea is that by forcing a conscious activity of this muscular structure under retrograde stress by pressure from his irrigating fluid that a sufficient contracture will follow, and control of the antigrade urine will result.

My experience has been that the problem is not so much a failure of activity of the external sphincter to resume its controlling capacity, but rather that the introduction of the element of scar tissue, particularly in perineal surgery, is an inhibiting factor against resumption of good control by the sphincter. In the case of retropubic and suprapubic methods it seems conceivable that the point of mooring by removal of the apical portion of the prostate leaves the prostatic capsule or scar tissue, if this structure has not been removed, to interfere with adequate closing of the urethra. In the case of resective surgery, distortion of the urinary channel where one portion of the prostate may have been more deeply resected than another (so that tortuosity results) I believe, accounts for failure of the sphincter to adequately close the urethral channel to such an extent, that loss of control often follows. Using retrograde force to encourage sphincter activity, if it really does this, may have its counterpart in the observation that many of us have made: when following a urethrocystogram on an incontinent postoperative patient, we have seen his control greatly improved. My impression has been that the sphincter has not been encouraged to exert better or more forceful control, but rather that better control has resulted perhaps from two reasons. One of these is that the lining of the channel may have been irritated enough to actually become more obstructive, and another that the retrograde column of fluid may actually straighten out the urethral channel in the operative field.

Oftimes I believe that we must search for causes other than local ones to explain the reasons for incontinence in postoperative patients. Very likely a simple neurological evaluation of the status of the patient will yield sufficient information to explain the loss of control. I believe that this should be carried out by the urologist, since only he is in a position to evaluate the quality of the controlling mechanism and the related neurological aberration. To explain more fully my concept of this, I believe that many in the elderly group, on whom we find it necessary to perform bladder neck surgery, have neurological abnormalities. Many of them will be found to have completely lost their vibratory sense, and almost all of them have lost the deep reflex mechanism of cremasteric or of abdominal muscular contraction. The external sphincter group of muscles is involved and made less efficient by the same mechanism. Consequently, we can hope for little return of function by mechanical stimulation. Rather these patients may require intensive and prolonged intrinsic factor therapy, either in the form of liver extract, vitamin, or folic acid therapy to improve this condition. Actually, a surprising and rather large proportion will be found to have sclerotic plaques in the spinal cord. When such exists, we cannot expect much from any type of therapy.

I should like also to mention the necessity of elimination by dilatation of the persistent element of scarring and secondary constriction which is usually seen in the posterior urethra following surgical procedures, other than resection, and in both areas of the urethra following the latter. Some operators have contended that short circuiting through the resectoscopic sheath may have been the cause of this, and others have felt that the prolonged use of an indwelling catheter has been the cause, the latter due to infection. Of course, many people have urethral strictures as a result of previous infection before any surgical intervention has taken place. For the past year I have made it a practice to lubricate the resectoscope sheath and indwelling catheters with water soluble sulfathiazole ointment and to asceptically bandage the penis, so that the catheter entering the meatus is protected. Such a practice has almost completely eliminated the element of stricture formation and relieves my mind from the possibility of oil emboli from the posterior urethra in case a petrolatum base was used. In closing I would like to reiterate the desirability of obtaining urethrocystograms on patients who are incontinent following surgery. It is a platitude to say that the more detailed our information of the abnormality, the greater our chances will be of correcting it. Still, it is certain that the problem is much involved and complicated and that it is one often amenable to cure by means other than clamps, bags, tubes, or pseudo-psychiatric manipulations. Dr. Vergés-Flaqué's efforts and plan are certainly steps in the right direction. I shall be anxious to hear further reports from him and will attempt to put his methods into practice.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

NEW MODALITIES IN UROLOGY[1]

JOSEPH FRANCIS McCARTHY

From the Department of Urology, New York Polyclinic Medical School and Hospital, New York, N. Y.

This communication illustrates the advantages to our profession of close collaboration between scientist and specialist. Of the several appliances to be here demonstrated, some of the original concepts came from my scientific co-worker, Mr. Frederick J. Wallace, of New York, N. Y.; others were the contribution of the writer. In this developmental work, we were greatly assisted by the scrutinizing criticism and the constructive suggestions of my associates, Drs. J. Sydney Ritter and Samuel E. Kramer.

As one of the chief offenders in the development of endoscopic prostatic resection and the endovesical management of certain types of bladder neoplasms, I have regarded it as obligatory to perfect, alter, or refine this highly technical instrument, insofar as seemed feasible.

The first modality here presented is what may be described as electronic or remote control of cutting and coagulating currents in the operation of prostatic resection (fig. 1). The cutting is regulated by finger pressure on a small red button. A white button, both built into the electrotome, regulates coagulation. Thus is eliminated the need of the awkward foot-switch which, in a darkened room, only a monkey could operate efficiently.

ADVANTAGES

This modality permits a saving of operating time, 10 to 15 minutes, with a reduction in blood loss. Finally, instantaneous finger-tip control of bleeding obviates, in large measure, the lens clouding in a bloody field, occasionally observed during clumsy foot-switch manipulation.

The second presentation is a diagnostic and operating retrograde telescope (fig. 2). This, we believe, will serve the useful purpose of precise retrospective visualization of the vesical aspect of the internal sphincter; the degree of intravesical prostatic encroachment, the thoroughness of the job, intravesically and intraurethrally, as well as the removal of residual tabs. It should afford a greater degree of precision at the beginning of the operation than heretofore available. The prompt and precise arrest of arteriolar bleeders at this point is also a feature. Furthermore, it will afford a visual appreciation of bladder tumors and a precision in management hitherto unobtainable.

During the course of this (years' long) research, we discovered a so-called blind spot in the foreoblique system of vision which is here corrected by reason of combined foreoblique and retrospective inspection. This telescope is equipped with the previously mentioned electronic controls. We have made many attempts at the difficult task of retrograde operative supplementation of foreoblique resection, none of which, according to our custom, have been released until supported by adequate clinical proof of utility. This is the most recent of our efforts in this direction.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

TECHNICAL DESCRIPTION

In this instrument, the loop movement is synchronous with that of the telescope. Therefore, the loop remains at all times in the middle of the visual field. There is no possibility of cutting beyond this field. In fact, because of its visual system, one observes the loop entering the sheath. It has been but recently completed, and is yet to be subjected to the acid test of adequate and detached clinical background. The complex lens system affords a 70 per cent visual field; an upright picture, and when moved laterally, requires no mental readjustment. Technically, the optical system incorporates a hemispherical prism, a Amici prism, a back lens, a series of achromatic lenses, a double inverting prism and an ocular. Finally, with the loop removed, it becomes at once an ideal exploratory instrument for retrograde inspection.

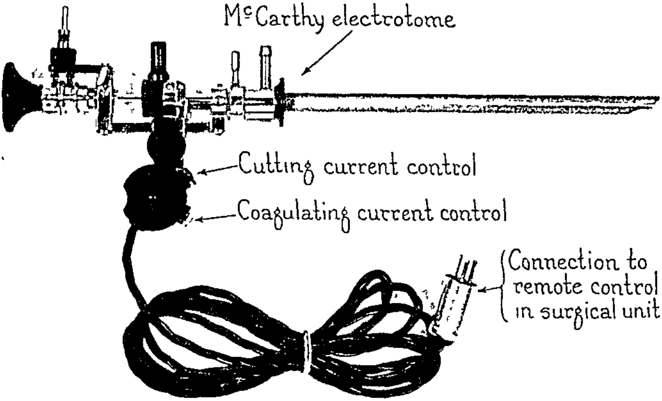

Mc Carthy electrotome
Cutting current control
Coagulating current control
Connection to remote control in surgical unit

FIG. 1. McCarthy electronic switch as applied to McCarthy electrotome

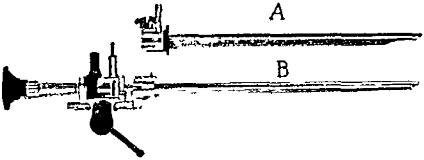


FIG. 2. *A*, Sheath for McCarthy electrotome. *B*, Working element consists of telescope, lamp and electrode. Telescope and electrode move simultaneously in retrospective direction.

The third gadget or combination of gadgets, is the incorporation of the before mentioned electronic controls in the already established insulated electrodes, with interchangeable cutting or coagulating terminals (fig. 3). These are intended for open bladder work but may also provide better controls in heminephrectomies and horseshoe kidneys. More important than this however, is the method of approach. Where a patient presents one or a number of growths, benign as well as certain types of malignancy, and where the position of such growths because of their location (superiorly or postero-inferiorly) are unsuited for endoscopic attack, the question of total cystectomy arises, at least for the malignant cases.

In this field there enters certain borderline cases as, in a recent one of epidermoid carcinoma (6 growths in all). The family declined total cystectomy and reimplantation of ureters. We were thus, as a matter of necessity, compelled to resort to the less radical one of cystotomy and electrical excision and coagulation. As the result of our experience in this case, we have come to the conclusion that the generally accepted method of cystotomy, retractors, internal illumination, etcetera, is inadequate for the proper management of such a case. Our practice here was, to completely mobilize the bladder, free it of its ligamentous and peritoneal attachments, and lay it wide open. Easy and precise attack was at once apparent. Some of the growths were on the trigone, others on the floor, and still others, on the mobile part of the bladder. The latter were completely excised; the former removed by a cutting loop down to the musculosa. With larger electrodes, the base and surrounding area were thoroughly coagulated. To avoid the possibility of pelvic cellulitis or injury to the subjacent structures, gauze packing was placed under the bladder. Before this patient's departure for home, there was no cystoscopic evidence of neoplasm in his bladder, and a centrifuged specimen of his early morning urine failed to reveal cancer cells.

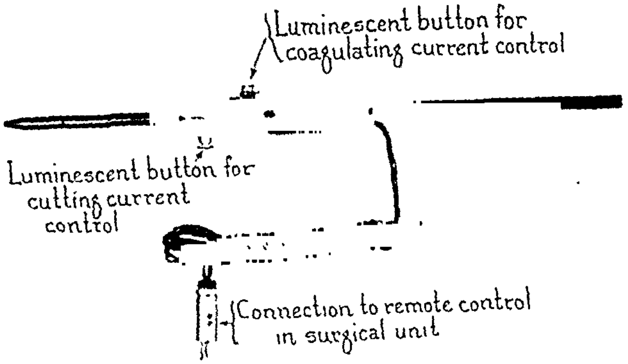

Luminescent button for coagulating current control
Luminescent button for cutting current control
Connection to remote control in surgical unit

FIG. 3. Bladder tumor electrode with McCarthy electronic switch attachment

This is certainly not presented as a replacement of the more radical, more effective total cystectomy and reimplantation of ureters, but in a limited field and under circumstances as before mentioned, it can serve an useful purpose. If it does, this is the way to do it.

The last in this presentation is shown here to call attention to the diverse possibilities in teaching, of the wire recorder, with some of which uses you are already familiar, such as wire recording of round table conferences. These recorded talks may be sent anywhere; repeated at will to the student body. Pedagogically it has the psychological impact of the speaker's personality. In the study of languages, and there never was a time when such knowledge is so necessary, it is quite unique.

It may open new avenues in teaching technique. Here, attempts have been made to magnify and record human heart sounds. This procedure has been essayed by others. The technique of reproducing these sounds and recording in this manner, is, we believe, a departure. In first efforts, the overtones seemed to mask the sounds sought. A witty cynic described it as an "African tom-tom". The present one seems a step in the right direction. We have discussed and speculated on these overtones. The thought arose that perhaps this highly sensitive receptor could possibly pick up heart muscle sounds not discernible through the stethoscope. With further technical refinements, and concurrent stethoscopic comparisons, this study may prove of some merit as a class teaching medium. Obviously, this exhibit is anything but a fait accompli. Should success attend these efforts, urologists may get to know as much about heart sounds as they think they know about prostates.

Other possibilities are the transmission of studies by members who have a message, throughout the English-speaking world, and later, the international field. It certainly can be made a factor for the international transmission of medical knowledge from us to them, and from our foreign friends to us, and in this manner, a harbinger of good will.

The modality last reported which concerns reproduction and recording of heart sounds, still rests in the field of speculation. This by no means carries an apologetic implication. There are in fact, a number of fantastic developments in the field of Urology that give promise of revolutionary changes in our present methods. Among these may be mentioned the direct endoscopic application of microwaves in the treatment of bladder tumors. The therapeutic possibilities of such microwaves of tremendously high frequencies, remains an unexplored field. If this isn't urologic day-dreaming, you name it.

Another is to apply the principle of electron optics. Here, the electro-magnetic lens may ultimately replace the ordinary lens systems of today, and the electron beam may equally well replace the light ray. Further, the electron picture thus produced, is projected on a sensitized screen. Bystanders may thus observe, as does the operator, a form of television, as it were, of growths in the bladder.

2 E. 54th St., New York 22, N. Y.

The Journal of Urology
Vol. 61, No. 1, January 1949
Printed in U.S.A.

DISCUSSION

DR. REED M. NESBIT (Ann Arbor, Mich.): Urology owes its existence as a specialty to the development of the cystoscope, and the preëminence of American urology today has, to a considerable degree, depended upon the genius and technical skill of two men, Reinhold Wappler, founder of the A.C.M.I., and his son, Frederick C. Wappler, who gave so generously of himself in the interests of urology, and to his country in her recent hour of desperate need.

Our genial elder statesman, Joseph McCarthy, has contributed many ideas for developments which have broadened the scope and usefulness of our armamentarium and today he has again demonstrated his ingenuity in the new modalities that he has described and which will no doubt make for better and more efficient technical urology.

In outlining some of the potentialities of electronoptics as they might be applied clinically, Mr. Frederick J. Wallace has opened up new and exciting areas for exploration. This man, trained as he is in the disciplines of the scientific attitude, has abundantly demonstrated himself to be a worthy successor to the Wapplers in the directing of the American Cystoscope Makers, Inc.

Before closing, I feel obliged to raise a word of caution to our genial friend, Joseph McCarthy. His modality for remote control of the high frequency currents is, of course, ingenious and will be useful, but his allusion to our simian ancestry is, I feel, a bit broad in its application, for we urologists have all been using the foot switch for these many years with great skill and dexterity; and now he says: "Thus is eliminated the need for the foot switch which, in a darkened room, only a monkey could operate efficiently." Is he trying to make monkeys out of all of us—or only those of us who henceforth use the foot switch?

DR. JOSEPH F. MCCARTHY (New York, N. Y.): My friend, Reed Nesbit, stole some of my thunder. I intended to talk about the Wapplers, father and. son, in closing the discussion. American Urology is what it is because of the Wapplers. Everybody knows that. What are all these visitors here to see? Surgical urology is pretty much the same the world over; instrumental technical urology is our particular pride.

Now, American Urology can be assured of the continuation of its high place by the co-operation of this man, Wallace, and his associates. In effect, this thing he has tried in different ways in electronics, amounts to television of the bladder.

The only thing I have to say in closing is to congratulate Reed Nesbit on his pedal facility, which seems to me, largely a matter of comparative proximity to one's anthropological forebears.

MR. FREDERICK J. WALLACE (New York, N. Y.): I am highly honored by the request to discuss the paper of Dr. J. F. McCarthy before this very distinguished gathering.

The principal contribution in any cooperative effort between Medicine and Technology is always made by the medical man. Without his inspiration and suggestions and final application of the end product, the technologist would be completely lost.

In the continuing development of an instrument suitable for retrograde resection, one of the problems has been to minimize the degree of re-orientation necessary on the part of the operator. This has been approached by instrument design which permitted the loop and objective to move simultaneously in the retrospective direction, and which provided an erect image inverted from right to left.

The application of electronic controls to the electrotome provides finger-tip control of the electrosurgical currents and eliminates the necessity of coordinating separate movements of hand and foot. The electronic switch comprises a three-wire circuit, one contact controlling cutting, one controlling coagulation, and the third a neutral wire. The cutting contact, when depressed, energizes a low voltage relay which, in turn, energizes the transformer primary, activates the transformer secondary completing the circuit of the vacuum tube or cutting current. The coagulating contact, when depressed, energizes a separate relay which activates a transformer and completes the spark gap or coagulating current. If both contacts are depressed simultaneously, a blended current is produced which both cuts and coagulates. The relays are extremely fast having a time delay of 1/1000 of one second. Application of both currents can be considered to be instantaneous.

The application, by means of instrumentation of ultra microfrequencies to neoplasms in the bladder, opens a field in which little or no work has been done. The ultra microfrequencies represent approximately that portion of the electro magnetic spectrum between 2000 and 100,000 megacycles frequency. No effective means of producing these frequencies with adequate power was available until the war-time development of the magnetron tube which permitted generation of a wide range of frequencies in pulsed or continuous form.

High frequency currents commonly used in electrosurgery for resection or fulguration of neoplasms occupy that portion of the electromagnetic spectrum between 5 and 43 megacycles. It is well known that some types of tumors are destroyed within the body by exposure to radiation in these frequencies. It seems apparent that an extensive field for investigation is open to determine the effects of the ultra micro waves in the still unexplored region of the electromagnetic spectrum between 2000 and 100,000 megacycles. Radiation energy of micro wave frequency cannot be conducted along wires or electrodes as in the case of radiation energies and lower frequencies. Hollow tubes or wave guides must be provided in the instruments for the transmission of the micro waves. Applied to the bladder through a cystoscope or panendoscope, the micro waves would be transmitted from the generator through a hollow tube to the site of the tissue being treated.

The possibility of applying the principles of electronoptics to urological instrumentation offers a field for experiment and investigation. In electronoptics the electron or beam of electrons replaces light rays and the electrostatic or electro magetic field replaces the optical lens. The electron beams are bent or focused to any desired path by electro magnetic or electrostatic fields placed at predetermined positions. The electron image of the object being viewed is projected on the face of a luminescent screen providing an enlarged visual image. With the development of improved techniques in electron optics, it may be possible in the future to visualize the interior of the bladder on a large viewing screen. In other words electron optics modified for application through instruments is in essence future television applied to cystoscopic procedures.

THE JOURNAL OF UROLOGY
Vol 61, No 1, January 1949
Printed in U S A

A CASE OF DOUBLE, TRIPLE, OR QUADRUPLE PENIS ASSOCIATED WITH DERMOID OF THE PERINEUM[1]

DAVID M DAVIS

From the Jefferson Medical College and Hospital, Philadelphia, Penna

A male child 7 weeks old was seen on November 5, 1946. Some small growths on the perineum had been observed at birth The baby had been apparently healthy and had gained weight normally

Examination showed a well nourished and well developed infant with no abnormalities discoverable except those of the genitalia and perineum (fig 1) In the normal position was a penis of normal size and contour, perfectly straight on erection. The prepuce was normal and retractable The meatus was normal in size and position, and clear urine was discharged in a stream of excellent size and force, with no leakage from any other point Beneath the penis was a bifid scrotum, each half of which contained a normal-feeling testis The scrotal halves were more widely separated posteriorly than anteriorly, and the space between them was occupied by a triangle of smooth, hairless skin Projecting from this area were three abnormal structures The first, which may be called structure A, was obviously a small penis, with well-formed glans, urethral meatus, and prepuce It lay in the line of a raphe, which ran from the base of the normal penis downward and diverging to the right, where it terminated in the region of the anus Beneath the skin the cylindrical shaft of structure A could be felt running down into the narrow angle between the crura of the corpora cavernosa of the normal penis, but one could not tell to which of them it was attached A probe entered the meatus for only a few millimeters

About 1 cm below and to the left of structure A was structure B, a small, flaccid tit-like projection, about 4 by 7 mm in size, in which no definite meatus could be seen There was no sign of glans or prepuce No shaft could be felt below the skin

About 1 cm further below and to the left of structure B was structure C. This again resembled a small penis, and was only slightly smaller than structure A As in structure A, there were a definite glans and a prepuce There was a depression at the tip of the glans, but the meatus, if present, was too small to admit a probe Beneath the skin a cylindrical shaft could be felt, disappearing into the space between the crura, but apparently attached to the left crus or descending pubic ramus.

The presence of these abnormal structures was associated with a good deal of excessive skin and subcutaneous fat, so that the anus was pushed to the right and the left buttock appeared much larger than the right The anus was small, admitting only the little finger with difficulty, but continent and otherwise normal. The prostate and seminal vesicles could not be definitely felt

In view of the undoubted male sex of the child, and the absence of any acces-

---

[1] Read at annual meeting, American Association of Genito Urinary Surgeons, Skytop, Pa , May 13, 1948

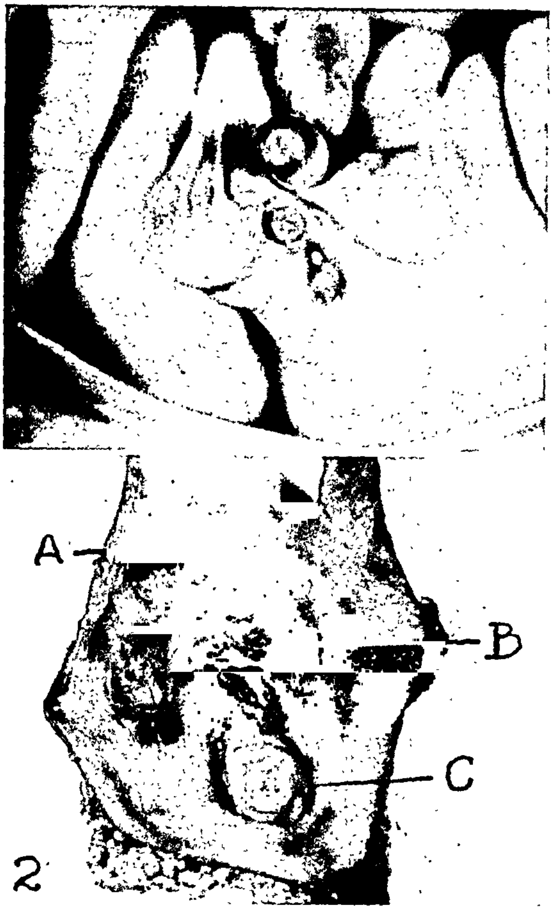


FIG. 1. *1*, View before operation. Note asymmetry of buttocks. *2*, Operative specimen. Letters show three abnormal structures.

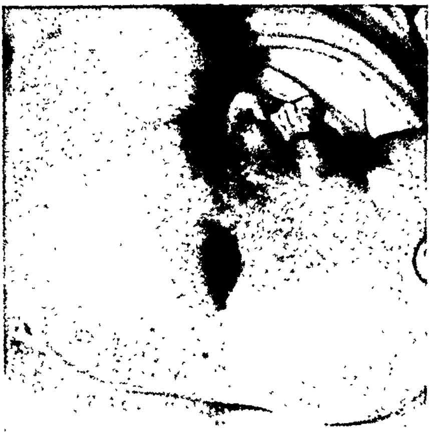


FIG. 2. Postoperative view. Asymmetry is partly corrected

sory urethral connections, it was decided that a simple excision of the abnormal structures, with plastic repair of the scrotum, was all that was necessary.

This operation was carried out on November 27, 1946. A No. 18 sound passed

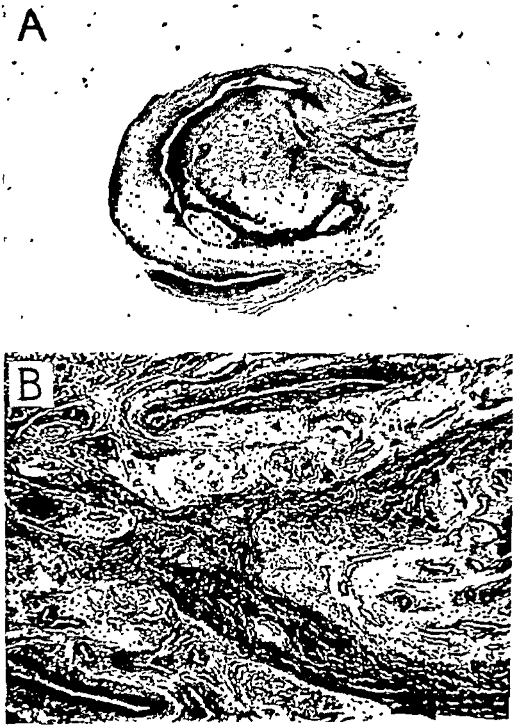


FIG. 3. Structure A. *A*, Longitudinal section showing prepuce, glans and corpora cavernosa. *B*, Higher power view showing erectile tissue.

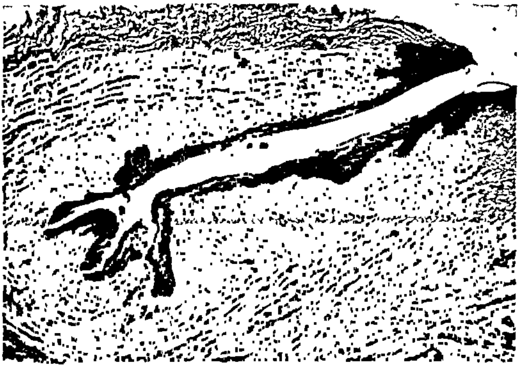


FIG. 4. Structure B. Longitudinal section showing sinus. Note epidermization in outer part.

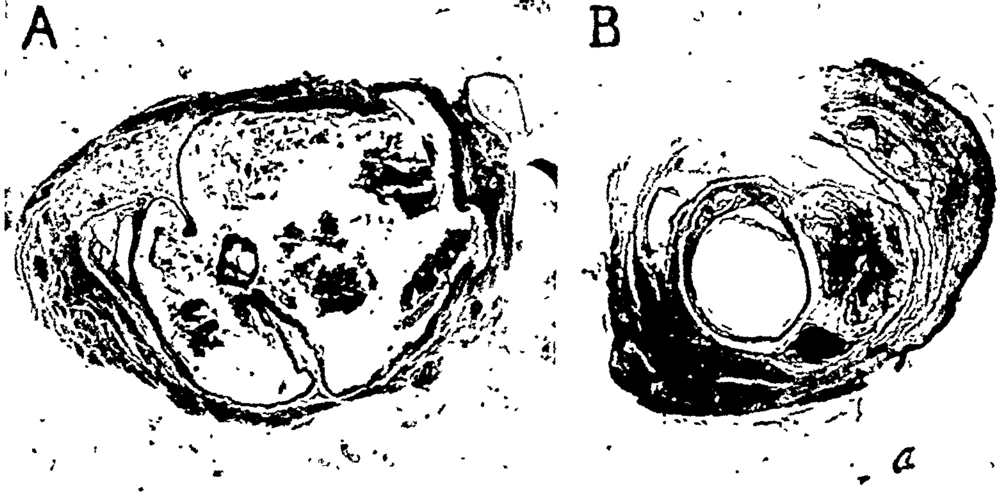


FIG. 5. Structure C. *A*, Cross section near tip showing large cyst, various kinds of epithelium and cartilage. *B*, Cross section of shaft showing smooth muscle and various kinds of epithelium.

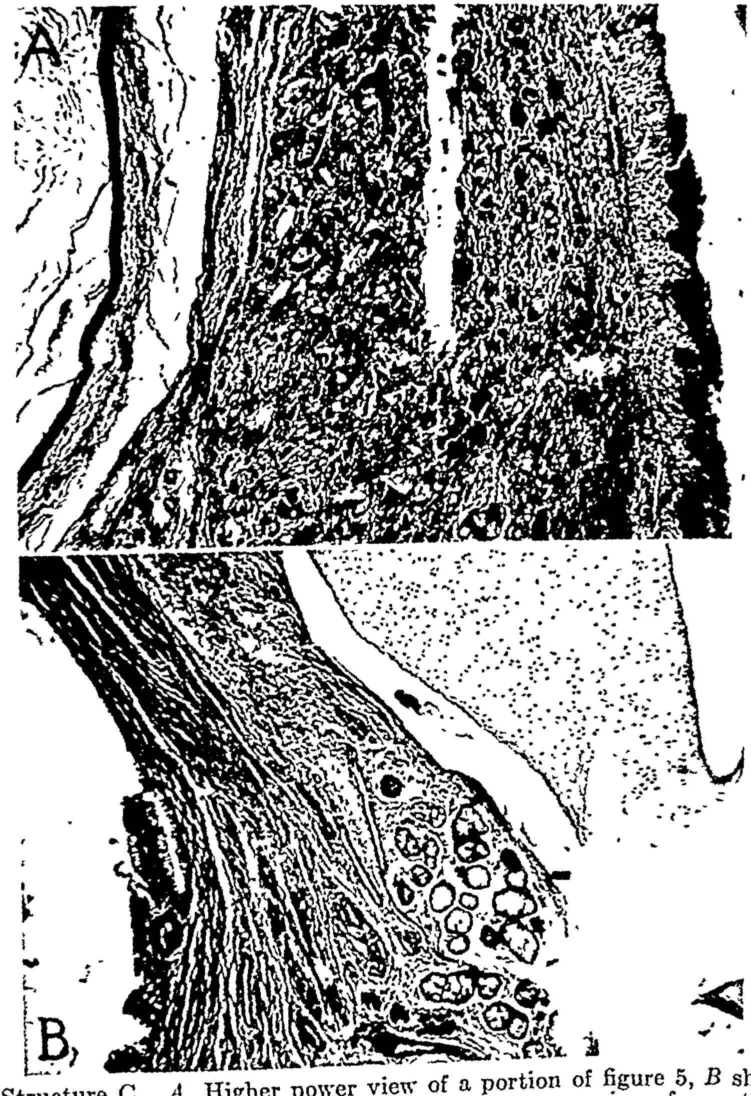


FIG. 6. Structure C. *A*, Higher power view of a portion of figure 5, *B* showing skin, cuboidal epithelium and group of giant cells. *B*, Higher power view of a portion of figure 5, *A* showing goblet cells, mucus glands, smooth muscle and cartilage.

easily to the bladder, and was kept in place during the operation to avoid any injury to the urethra. The incision was generally diamond-shaped, in order to remove a wedge of skin and fat and thus reduce the size of the left buttock. It passed a little distance into each scrotal half, and included all the smooth skin between the scrotal halves. The operative specimen is shown in figure 1, *B*.

Beneath the skin the shafts of structure A and structure C were found to converge toward the left and join near the left descending pubic ramus, to which they were attached close to the tip of the crus of the left corpus cavernosum of the normal penis. They were ligated as close to the bone as possible and cut off. No shaft leading to structure B could be found.

The scrotal halves were then drawn together by many individual sutures of 5-0 chromic catgut, and the skin closed with a continuous right-angle mattress suture of fine black silk. This produced a scrotum of practically normal appearance. The incision healed per primam, and the patient left the hospital 8 days after the operation. The final result is shown in figure 2.

Section of structure A showed that it was indeed an accessory penis, with prepuce, glans, and corpora cavernosa (fig. 3, *A*). That the glans and corpora are composed of erectile tissue is shown in figure 3, *B*, taken at a higher magnification.

In structure B no erectile tissue could be identified, but there was a deep sinus lined with epithelium (fig. 4) which suggested strongly an attempt to form a urethra. In the outer part of this sinus epidermization was present, but in the deeper parts the epithelium appeared to be of the transitional type.

In structure C the findings were surprising. Figure 5, *A* shows a cross-section of what appeared to be glans. Actually it was a thin layer of tissue surrounding a large irregular cystic cavity filled with gelatinous cellular debris. The tissues present represented entodermal, mesodermal and epidermal elements. Figure 5, *B* shows a cross-section of the deeper part of the shaft. Figure 6, *A* shows, entodermal more highly magnified, an area of figure 5, *B* in which many large giant cells are present in a connective tissue stroma. Figure 6, *B* is a higher magnification of a portion of figure 5, *A*. The cyst is lined with thin cuboidal epithelium, while a gland-like structure emptying into it is lined with mucus-bearing columnar cells recalling those of the large intestine. Similar cells line a group of acini outside the smooth muscle surrounding the cyst. In the upper right corner of the section is a large area of typical cartilage. Structure C, therefore, while having an external appearance suggesting a penis, is really embryomatous in character, and justifies, I believe, the appellation teratoma or dermoid.

The child was seen 10 months after operation, at which time there was no sign of any recurrence of neoplasm. On May 10, 1948, nearly 18 months after operation, his mother reported that he had remained perfectly well.

I must leave the decision as to whether this case represents double, triple, or quadruple penis to my readers. In any event, it is, I believe, unique.

The Journal of Urology
Vol. 61, No. 1, January 1949
Printed in U.S.A.

THE TREATMENT OF HYPOSPADIAS[1]

AUSTIN I. DODSON

From the Urological Department, St. Elizabeth's Hospital, Richmond, Va.

Hypospadias is one of the most frequent of congenital deformities. It may occur in such minor degrees that it is barely noticeable or may be so extensive that the sex of the child at birth is in doubt (fig. 1, *A*). The failure of complete development of the urethra results in congenital fibrosis of the corpus spongiosum distal to the hypospadic orifice and a consequent downward curvature of the penis (fig. 1, *B*). Treatment has the dual purpose of correcting the deformity of the penis and establishing the undeveloped portion of the urethral channel.

The first step in the treatment of hypospadias is straightening the penis. This operation should be done at an early age so that the penis will develop normally. Particularly is this true in the more pronounced degrees of hypospadias where normal development is definitely retarded by the ventral fibrosis and complete correction is more difficult in older children. In my own practice when possible the first operation is done before the child is 2 years old. In young children the first operation should be devoted entirely to correcting the penile deformity (fig. 2, *A*). In older children and in adults, I have combined the straightening operation with the formation of a channel through the glans penis by a tubular graft from the skin of the prepuce as devised by D. M. Davis (fig. 2, *B*). This not only simplifies the final construction of the urethra but also aids in holding the penis straight while healing. The operation for straightening the penis is usually begun by making a transverse incision on the under surface of the penis a short distance from the hypospadic opening. Buck's fascia should be divided and all constricting fibrous tissue should be dissected away from the hypospadic opening to the base of the glans. These bands of fibrous tissue will be situated mostly between and along the ventro-lateral margins of the corpora cavernosa. The dissection should extend back beneath the terminal portion of the urethra for a short distance. In advanced degrees of hypospadias, it is better to make two transverse incisions, one just anterior to the hypospadic opening and one just posterior to the base of the glans penis. When the dissection is complete, all bleeding is carefully controlled and the fascia and skin of the penis are closed in the opposite direction of the incision. The penis should then be inspected and if the skin appears to constrict the penis, short longitudinal incisions may be made on the dorsum of the penis and sutured in the opposite direction, thereby relaxing the skin. This aids healing and has a tendency to shift skin from the dorsal to the ventral surface of the penis for future need in constructing the urethra. Occasionally the fibrosis seems to involve the adjacent skin to the extent that when the penis has been straightened there is not sufficient healthy skin to cover the defect. In such cases the prepuce may be transferred to the ventral surface of the penis as suggested by Edmunds,

---

[1] Read at annual meeting, Southeastern Section, American Urological Association, Hollywood, Fla., January 9, 1948.

Blair and Nesbit. I prefer to leave the prepuce undisturbed if possible. It is frequently useful in constructing the urethra. I have found it helpful to keep the penis straight while healing by suturing the glans to the skin of the abdomen by a single course silk suture. The wound is covered with sulfathiazole ointment and a light dressing applied with moderate pressure. A small catheter is left in place for about 48 hours after which an apron of gauze is attached to the lower abdomen with adhesive tape to protect the wound. The patient is hospitalized from a week to 01 days for this operation.

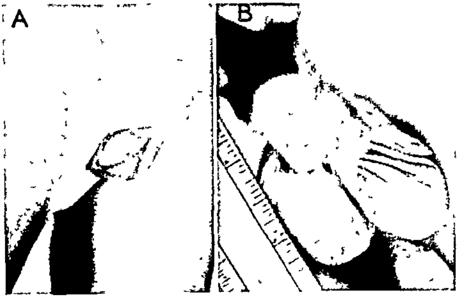


FIG. 1. *A*, left, Perineal hypospadias with bifid scrotum and pronounced downward curvature of penis. *B*, right, penoscrotal hypospadias with moderate deformity.

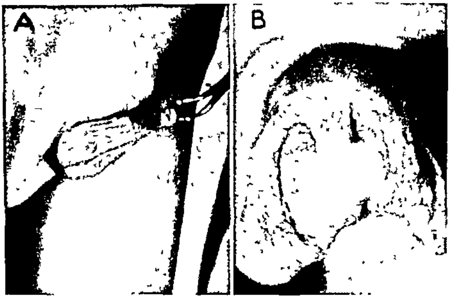


FIG. 2. *A*, left, Twelve months following operation to straighten penis. Patient has returned for construction of urethra. (Same patient as figure 1, *A*.) *B*, right, Urethra extended through glans penis by method of D. M. Davis. Healing is complete. Pedicle may now be divided.

I prefer to construct the urethra when possible before the child enters school. The urine must be diverted either by perineal urethrostomy or by suprapubic cystostomy. In perineal hypospadias, the hypospadic opening serves for drainage while the penile portion of the urethra is being constructed. When the anterior urethra is completely healed, the perineal defect may be closed over a small catheter which is left indwelling for drainage. Considerable tissue can be closed over the repair and fistulas are not so troublesome in this area. If one prefers, the urine may be diverted for this final operation by suprapubic cystostomy. When the urethra opens anterior to the perineum, a perineal urethrostomy is the best method of drainage. In small children with considerable deformity, a perineal fistula may be made by extending the incision in the urethra about a half an inch and suturing the mucous membrane to the skin. When this is done it is not necessary to keep a catheter in place, consequently there is less danger of infection of the urinary tract and repeated urethrostomy is avoided when several operations are necessary. The fistula is easily closed when a satisfactory urethra has been established. In most cases, a perineal urethrostomy with catheter drainage is preferred. A ligature of coarse silk or silk worm gut tied around the urethra just anterior to the urethrostomy incision is an added precaution against wound contamination. If the ligature is tied just tightly enough to occlude the urethra, it will not cut through.

Numerous methods of constructing the urethra have been described. The appendix, the ureter, the saphenous vein and tubes constructed from the mucosa of the bladder and the skin have been utilized. In most cases these free transplants have not been very satisfactory. The transplanted tissue often sloughs or is absorbed. At best a constricted tube results which must be repeatedly dilated to maintain a semblance of a urethra. The least complicated operations are more apt to be successful. The most satisfactory results have been obtained by the use of pedicle grafts. The principles involved in pedicle grafts are embodied in the operations described by Thiersch, Bucknall and Ombredanne. These operations modified according to the problem at hand are likely to be successful. No one method can be applied to all cases. The technique of these operations are familiar or can be more satisfactorily obtained from the original articles or from the very excellent review of the subject by Cecil. They will not be repeated here.

I prefer the Thiersch method of reconstructing the urethra whenever it can be applied. The urethra is constructed from the skin of the penis with the roof of the urethra left attached along the surface of the penis; therefore, there is no doubt that the canal will develop with the development of the penis. A broad base insures an adequate blood supply and the line of sutures for constructing the urethra and the sutures for closing the skin flap over the urethra are not opposite each other, therefore, fistulas are relatively infrequent. If there is not enough skin left after constructing the urethra to close the defect without tension on the sutures, the prepuce may be used to cover the defect or if it has been removed the operation may be continued by utilizing Cecil's modification of the Bucknall operation or by using a skin flap from the scrotum as recommended by Blair. The Thiersch operation has been used successfully in more than three-fourths of 60 patients operated upon for hypospadias during the past 10 years (fig. 3).

The Bucknall operation is usually successful. There is the assurance of adequate blood supply and postoperative fistulas are rare. A portion of the urethra is formed from scrotal skin, creating a possible hazzard from the growth of hairs into the urethra. This disadvantage is overcome by Cecil's modification in which the urethra is formed from the skin of the penis by dissecting up longitudinal flaps to form a tube. A longitudinal incision is then made in the scrotum and the new formed urethra is buried in the scrotum by suturing the margins of the scrotal incision to the margins of the wound on the ventral surface of the penis. When the wound is healed the penis is dissected from the scrotum and the operation completed as in the original Bucknall operation. In both the Thiersch and the Bucknall operations, the newly formed urethra terminates in the region of the frenum. This gives satisfactory functional results but falls somewhat short of the perfection desired by most patients and particularly by the parents of young children.

The most satisfactory method of carrying the urethra to the end of the penis is the use of the pedicle tube graft devised by D. M. Davis. This tube graft, as illustrated in figure 4 may be used with the Thiersch or Dupley operation to extend the urethra through the glans or may be used alone to correct the lesser degrees of hypospadias. I have used it successfully in cases of penile hypospadias. With the base of the tube graft toward the base of the penis, the blood supply is adequate and the graft can be made as long as the length of the penile skin will allow. As previously mentioned, I frequently construct the glandular portion of the urethra at the time that the penis is straightened.

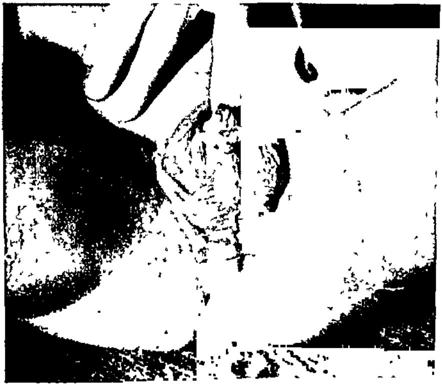


FIG. 3. Perineal hypospadias corrected by combining the Thiersch and Davis operations

In penile and penoscrotal hypospadias, the Ombredanne operation gives a rather poor cosmetic result, and in addition there is the disadvantage that scrotal skin is used to line a portion of the urethra. I have used the Ombredanne operation in very minor degrees of hypospadias. Regardless of the fact that a hypospadic opening situated at or near the frenum rarely interferes with normal function, the patient or the patient's parents are frequently definitely disturbed because of the minor defect. In most cases of this type, there is a slight ventral groove in the glans. I find that the Ombredanne method can be applied in such cases very satisfactorily advancing the meatus almost to the tip of the penis. I usually leave a small catheter in for drainage 2 or 3 days. If the frenal hypospadias is accompanied by deformity of the penis, the operation is done in two stages using the pedicle tube graft to construct the urethra.

Many types of suture material have been recommended. I have had better results with catgut. For the construction of the urethra fine plain catgut usually 000 is used. The sutures must be carefully placed so that the skin edges will be turned in. A more even tension can be secured by using interrupted sutures. Fine chromic catgut or silk is used for the superficial sutures. In small children chromic catgut is more satisfactory.

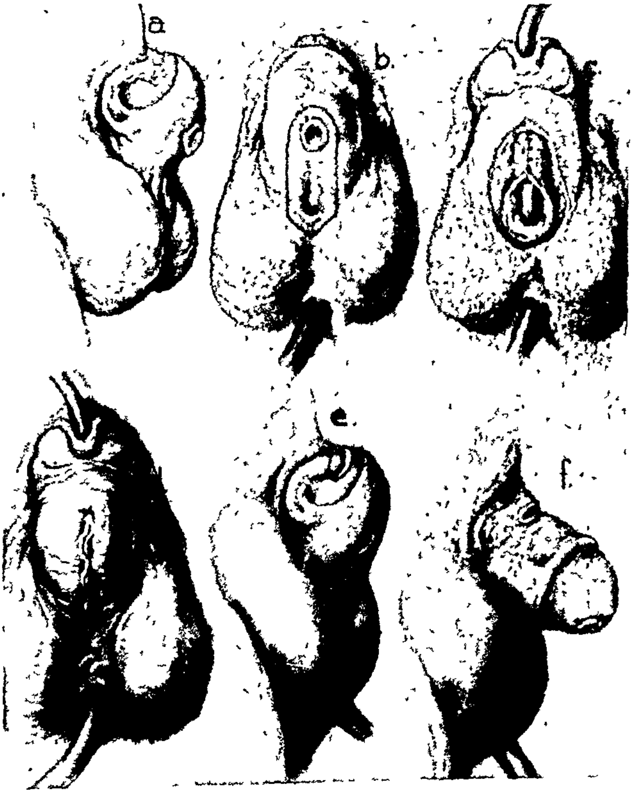


Fig. 4. Different steps in combining operation of D. M. Davis and of Thiersch for correction of penoscrotal hypospadias. *a*, Tube graft drawn through glans penis. *b*, Orifices of tube graft and hypospadic urethra with outline for forming remaining portion of urethra. *c*, Urethra partially sutured. *d*, Closure of urethra is complete. *e*, Lateral view of same. *f*, Tube graft has been excised.

Most operations for the correction of hypospadias fail because the principles underlying plastic surgery are neglected. An adequate blood supply is most important. A broad pedicle should be left for the nourishment of flaps which should be dissected just far enough to be accurately approximated without tension. In outlining flaps and grafts, it is important to remember that the skin of the penis and scrotum shrinks considerably when dissected free. Efforts to construct and to cover the urethra with inadequate skin flaps result in excessive tension on the sutures. Consequently, the blood supply along the suture line is diminished and healing is retarded. Absolute hemostasis is also important; even the most minute bleeding point should be ligated. Wherever blood clots form fistulas are apt to occur.

Postoperative care is most important. A dressing is applied with moderate pressure. A soft sea sponge applied over a few layers of gauze and held in place with adhesive provides even, elastic pressure. Sulfathiazole ointment coated over the wound will prevent the gauze from sticking. The catheter should be accurately adjusted. If the catheter projects into the bladder too far or is pulled into the posterior urethra, bladder spasm is apt to expel urine around the catheter. Until healing is complete, the drainage tube requires constant care. The slightest evidence of poor drainage or bladder discomfort requires immediate attention. Contamination of the wound with urine especially through the newly formed channel usually causes at least a partial break down of the suture line. It is well to change the catheter at the end of a week. Deposits of salts from the urine may gradually occlude the catheter. Bladder drainage should be continued until the wound is entirely healed or until it is evident that the operation is not entirely successful. If the patient has passed puberty, I administer stilbestrol. Troublesome erections are much less frequent. Infections of the wounds and of the urinary tract are rarely encountered when penicillin and sulfacetamide are used prophylactically. I prefer to change the dressing in about 48 hours. If there has been subcutaneous bleeding the blood can, at times, be evacuated before trouble is caused or edematous areas can be pricked with a pointed knife reducing tension. Subsequent dressings are applied without pressure. A minimum of two weeks is required for complete healing. When a portion of the wound breaks down, the defect should not be repaired for a period of 6 months.

166 E. Franklin St., Richmond, Va.

REFERENCES

Blair, V. P. and Byars, L. T.: Hypospadias and epispadias. J. Urol., 40: 814–25, 1938.

Cecil, A. B.: Surgery of hypospadias and epispadias in the male. J. Urol., 27: 505–37, 1932.

Cecil, A. B.: Repair of hypospadias and urethral fistulae. J. Urol., 56: 237–242, 1946.

[illegible] ADDEN, W. S.: Hypospadias. J. Urol., 49: 444–9, 1943.

[illegible] rgery, St. Louis, C. V. Mosby Co., 1944.

[illegible] Ombredanne operation for the repair of penile hypospadias. J. Urol., 56: 746–756, 1946.

Young, H. H.: The abnormalities and plastic surgery of the lower urogenital tract. J. Urol., 35: 417–480, 1936.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

STREPTOMYCIN THERAPY IN UROGENITAL TUBERCULOSIS[1]

LEON HERMAN

Notwithstanding meager data on the subject, I have chosen to discuss with you the influence of streptomycin on urogenital infections with special reference to tuberculosis. The latter, once a very common manifestation of the disease, has shown progressive decline in all parts of North America with the possible exception of certain parts of Canada and Alaska. Indeed, it is now difficult to find enough clinical material for teaching purposes, and in response to a questionnaire, urologists from widely separated parts of the country attribute their lack of experience with streptomycin therapy to lack of cases. Nevertheless urogenital tuberculosis is still with us, but often, it seems to me, in modified form.

Chronicity and intermittency of its clinical symptoms have always been characteristic of the disease, but I believe that factors promoting its disappearance have added to its essential chronicity. The physician must be more alert than ever before to suspect tuberculosis as the cause of slight vesical irritability associated with microscopic pyuria. In illustration of this, I cite one of several cases in which insignificant ulceration of the bladder typical of that associated with interstitial cystitis, proved to be tuberculous in origin.

A woman aged 45 consulted us in June 1943, complaining of great frequency and urgency of urination. The urine contained an occasional leukocyte. The trouble began in 1940 when she consulted a gynecologist who irrigated the kidney pelves every 2 weeks for a period of 2 years without relief. She then consulted an urologist who made the diagnosis of Hunner's ulcers which were treated twice by electrocoagulation, with slight improvement. Our examination disclosed a large ulcer situated behind the left ureteral orifice and two smaller ulcers behind the right ureteral orifice. The ulcers were characteristic of the type associated with interstitial cystitis. The patient was greatly improved by mild electrocoagulation of the ulcers. However in October 1946 she had a sudden attack of severe pain in the left kidney region with return of her bladder symptoms, which had entirely disappeared for a period of 1½ years. This was the initial symptom of upper urinary tract origin. The left kidney, which was tuberculous, was removed in November 1946 and the patient is now symptom free and the ulcers healed.

The first mention of streptomycin is to be found in the January 1944 issue of the *Proceedings of the Society of Experimental Biology and Medicine.* This fungoid antibiotic isolated by Shatz, Bugie and Waksman was found to inhibit the in vitro growth of various organisms, including the tubercle bacillus. Effective bacteriostatic effects on the human tubercle bacillus in vitro were noted with high dilutions and the growth of the bacillus completely arrested in concentrations of 100 units per cubic centimeter.

As Shatz and Waksman and others have shown, streptomycin protects guinea pigs against inoculations with this bacterium. Youmans and McCarter after inoculating 30 mice with human virulent tubercle bacilli, and using 15 of the animals as controls, gave each of the remaining fifteen, 3,000 units of streptomycin daily, in divided doses. After 28 days, only 13 of the inoculated animals were alive and these had massive pulmonary tuberculosis. Of the treated animals, 87 per cent were alive and apparently well, although at necropsy scattered microscopic infiltration was found in the lungs of some of these. The results of these and other investigations raised the hope that streptomycin would prove destructive to organisms unaffected by penicillin, and while experience supports the modest claims of the originators of streptomycin the hope of Ehrlich of Sterilisans magna remains unfulfilled. Perhaps it was unreasonable to hope that the efficient protective action of streptomycin on innoculated laboratory animals would be duplicated in clinical work, since streptomycin, like all other blood borne therapeutic agents, is largely excluded from the avascular portions of chronic sclerosing and necrotizing lesions of which tuberculosis is a classical example. This is certainly true of chronic tuberculous lesions of the kidney and especially of the caseocavernous types, notwithstanding the elimination of from 25 to 67 per cent of streptomycin by the kidneys during a 24 hour period. If it is true, as Medlar originally claimed, that unilateral surgical tuberculosis of the kidney merely represents the end results of a once widespread infection of both kidneys, it is conceiveable that streptomycin therapy might serve to minimize the danger of activation of the disease in the apparently healthy kidney.

---

[1] Read at meeting of Puerto Rican Medical Association, December 1947. Also as the Ballenger Lecture read at annual meeting, Southeastern Section, American Urological Association, Hollywood, Fla., January 8, 1948.

Gilbert Thomas, who has long advocated preliminary medical care of patients who are to undergo nephrectomy for supposed unilateral tuberculosis, calls attention to the study of tissues obtained at autopsy from patients who had had adequate treatment with streptomycin. These studies show that the small and early, rather than the large, chronic lesions of tuberculosis respond to treatment, and the probabilities are that the curability of renal tuberculosis by operation will be increased by preoperative destruction by streptomycin of minimal lesions in the apparently healthy kidney, which so often become grossly involved after operation and possibly because of the trauma incident to it. Unlike penicillin, which occurs in molecular series exhibiting different degrees of antibiotic activity, streptomycin is uniform, notwithstanding wide variability in its bacteriostatic activity in vivo against susceptible organisms which may be attributable to mechanical rather than to biological factors. It is desirable in clinical work to adopt a standard of in vitro susceptibility, but it must be remembered that improvement may follow streptomycin therapy in cases in which such tests show high bacterial resistance. Sensitivity studies are of little practical value in tuberculosis, owing to the slow growth of the tubercle bacillus on artificial media. Buggs and his co-workers have shown that the tubercle bacillus acquires enduring and effective resistance to streptomycin which Youman's estimated to be from 500 to 1000 times in human. Olsen states that this resistance may be delayed or decreased and the action of streptomycin enhanced by the addition of penicillin therapy, while Smith advocates the use of sulfones in conjunction with streptomycin. This evidence of synergistic action needs further study.

of the tubercle bacillus obtained from the sputum and urine of patients, prior to streptomycin therapy, were sensitive to concentrations of 3 micrograms of streptomycin per cubic centimeter in vitro, and the vast majority, to 1 microgram per cubic centimeter or even less. It is further stated that with the dosage of 1.8 to 2 gm. daily, concentrations of streptomycin in the circulating blood plasma does not fall below 5 micrograms per cubic centimeter so that at the outset of treatment therapeutically high blood levels are present. The dosage now advocated by the Veterans Bureau is 1 gm. daily and I am informed that reduction of the daily dosage to ½ gm. is under consideration. In vitro tests have disclosed acquired resistance of the organisms to streptomycin as treatment continues and it is reasonable to suppose that resistance in vitro means resistance in vivo, but it is impracticable as yet to take full advantage of this knowledge.

We have used either 1.8 or 2 gm. streptomycin daily in our cases of tuberculosis in divided doses at 3 hour intervals. The toxic reactions with the exception of slight vestibular reactions have been few. Attention may be called to a case in which severe anaphylactic reactions occurred after 4 days' treatment with combined penicillin and streptomycin. The reaction, which lasted 2 weeks, was characterized by fever, marked swelling of the face and extremities and large multiple wheals. In one of our cases, and in several reported instances, severe renal pain occurred, due apparently to local action of streptomycin, which is a renal irritant and may cause damage to the kidneys. Gross hematuria has not been observed while microscopic blood casts and albumin are not infrequently found. These are not serious unless there is increasing retention of blood urea nitrogen which would necessitate stoppage of treatment. Involvement of the auditory branch of the eighth nerve leading to permanent deafness is a rare but definite hazard. We have observed severe vertigo with diplopia.

PERSONAL EXPERIENCE

Of the 8 cases of urogenital tuberculosis treated with streptomycin under our observation, 3 present features of special interest.

In the first case, an acute tuberculous epididymal abscess developed during treatment. The second case is one of very early unilateral renal tuberculosis and possibly the only one of its kind thus far subjected to streptomycin therapy. The third case is representative of the results obtainable in most cases of ancient bilateral renal tuberculosis, in that the urine was promptly freed of tubercle bacilli, but this proved to be only temporary.

Case 1. A man aged 31 was first seen by us in 1930, when he complained of right flank pain and gross hematuria. The diagnosis of unilateral (right) renal tuberculosis was made and nephrectomy advised. The patient was not heard from again until 1939 when he returned for re-examination in anticipation of marriage. With the exception of slight frequency he was symptom free. Examination disclosed a well healed lesion in the region of the right ureteral orifice and a large tuberculous pyonephrosis, on the right side. The left kidney was normal. The right kidney was removed. The patient remained in good health, having been married in the meantime. He was the father of 2 children, which is pigs against inoculations with this bacterium. Youmans and McCarter after inoculating 30 mice with human virulent tubercle bacilli, and using 15 of the animals as controls, gave each of the remaining fifteen, 3,000 units of streptomycin daily, in divided doses. After 28 days, only 13 of the inoculated animals were alive and these had massive pulmonary tuberculosis. Of the treated animals, 87 per cent were alive and apparently well, although at necropsy scattered microscopic infiltration was found in the lungs of some of these. The results of these and other investigations raised the hope that streptomycin would prove destructive to organisms unaffected by penicillin, and while experience supports the modest claims of the originators of streptomycin the hope of Ehrlich of Sterilisans magna remains unfulfilled. Perhaps it was unreasonable to hope that the efficient protective action of streptomycin on innoculated laboratory animals would be duplicated in clinical work, since streptomycin, like all other blood borne therapeutic agents, is largely excluded from the avascular portions of chronic sclerosing and necrotizing lesions of which tuberculosis is a classical example. This is certainly true of chronic tuberculous lesions of the kidney and especially of the caseocavernous types, notwithstanding the elimination of from 25 to 67 per cent of streptomycin by the kidneys during a 24 hour period. If it is true, as Medlar originally claimed, that unilateral surgical tuberculosis of the kidney merely represents the end results of a once widespread infection of both kidneys, it is conceiveable that streptomycin therapy might serve to minimize the danger of activation of the disease in the apparently healthy kidney.

Gilbert Thomas, who has long advocated preliminary medical care of patients who are to undergo nephrectomy for supposed unilateral tuberculosis, calls attention to the study of tissues obtained at autopsy from patients who had had adequate treatment with streptomycin. These studies show that the small and early, rather than the large, chronic lesions of tuberculosis respond to treatment, and the probabilities are that the curability of renal tuberculosis by operation will be increased by preoperative destruction by streptomycin of minimal lesions in the apparently healthy kidney, which so often become grossly involved after operation and possibly because of the trauma incident to it. Unlike penicillin, which occurs in molecular series exhibiting different degrees of antibiotic activity, streptomycin is uniform, notwithstanding wide variability in its bacteriostatic activity in vivo against susceptible organisms which may be attributable to mechanical rather than to biological factors. It is desirable in clinical work to adopt a standard of in vitro susceptibility, but it must be remembered that improvement may follow streptomycin therapy in cases in which such tests show high bacterial resistance. Sensitivity studies are of little practical value in tuberculosis, owing to the slow growth of the tubercle bacillus on artificial media. Buggs and his co-workers have shown that the tubercle bacillus acquires enduring and effective resistance to streptomycin which Youman's estimated to be from 500 to 1000 times in human. Olsen states that this resistance may be delayed or decreased and the action of streptomycin enhanced by the addition of penicillin therapy, while Smith advocates the use of sulfones in conjunction with streptomycin. This evidence of synergistic action needs further study.

The literature contains a number of reports on the clinical use of streptomycin in urogenital tuberculosis. Thus in the *Proceedings of the Staff Meetings of the Mayo Clinic* for September 1945, Hinshaw and Feldman discuss a series of 34 cases of tuberculosis of various organs including 5 in which one kidney had been removed with persistence of tubercle bacilluria. In 4 of these cases the bacilli disappeared from the urine after 2 to 4 weeks of treatment, and cultures were sterile from 1 to 4 months after cessation of treatment. In 1 patient the urine remained positive for the tubercle bacillus but there was pyelographic evidence of healing of the renal lesions. These same writers later reviewed 9 cases of renal tuberculosis, in 8 of which the urine was freed of tubercle bacilli with definite improvement of symptoms, but the bacilli reappeared in 6 cases after the cessation of treatment. In many of these cases cystoscopy disclosed healed or healing vesical lesions. In July 1946, Cooke, Greene, and Hinshaw described 7 cases, adding these for statistical purposes to the 5 previously reported. In this series the disease was either bilateral, or one kidney had been removed for tuberculosis, and in each case the bladder was involved. Of these 12 cases streptomycin therapy brought relief from the bladder symptoms in 6 instances, and of those unrelieved, 3 showed evidence of healing of the bladder ulcerations. Only 2 cases gave negative guinea pig tests. These observations accurately foreshadowed the results of additional experience. Undoubtedly streptomycin has a powerful bacteriostatic effect on the human tubercle bacillus in vivo but it is rarely curative, and recurrent bacilluria in urogenital cases is the rule. In confirmation of this we quote from the *Medical Bulletin of the Veterans Administration* for August 1947 in which a series of 39 cases of urogenital tuberculosis with multiple lesions and positive urine cultures are described in detail. Of these, 13 had completed 120 days of therapy by August 1947, having been studied before, during and after treatment. Nine of the 13 showed considerable, although occasionally temporary improvement in bladder irritability with increased capacity in 10, and improvement on cystoscopic examination in 11. Epididymal sinuses healed in 3 cases while 23 of 32 lesions of the posterior urethra and adnexal sexual glands improved. We have noted the almost complete disappearance of palpable evidence of the disease in 1 case of extensive tuberculosis of the prostate gland and seminal vesicles after streptomycin therapy, comparable with the results occasionally obtained with stilbesterol therapy in extensive carcinoma of these organs.

Redewell reports 2 cases of residual vesical tuberculosis treated successfully with a combination of streptomycin and iontophoresis. The latter comprises the use of quartz light applied to the bladder partially filled with a solution of streptomycin through a specially devised instrument. Finally Mathé reports symptomatic relief in 4 advanced cases and while he conceded the powerful action of streptomycin, holds with the majority of writers that it is rarely if ever curative of urogenital tuberculosis.

A method of treatment devised by Slotkin may have considerable importance in the future therapy of tuberculosis. This investigator conceived the idea that the waxy cell wall surrounding the tubercle bacillus explains part of the resistance of the organism, attributing the action of chaulmoogra oil in leprosy to its solvent action on similar protective cell wall. He used the agent in the treatment of a few cases of urogenital tuberculosis 10 years ago but the preparation employed was unsatisfactory. The treatment was again started in January 1947, using a purified chaulmoogra oil and one supplied by Burroughs Wellcome Co., with the trade name "Moogrol"; the latter preparation is stable, readily absorbable and nonirritating. After adequate laboratory investigations Slotkin began the clinical use of these oils in combination with streptomycin and in a preliminary report cites the results of treatment in 6 advanced cases of tuberculosis of the urogenital organs. The clinical results in the small series indicate a powerful action of this combination of agents against the tubercle bacillus; in fact they are superior to those obtained by any method hitherto employed although the series is too small and the elapsed time too short for true evaluation of the method.

DOSAGE AND TOXICITY

Streptomycin is available in the form of hydrochloride, sulphate and phosphate salts, and calcium chloride complex. The unstandardized material originally used is said to be more efficient, but it is more productive of reactions than the purified materials, although as experience has shown, toxic reactions commonly follow the use of the latter. Streptomycin is freely soluble in water and aqueous solutions may be kept at room temperature for a week without losing activity, and for months under refrigeration. Solutions are said to lose 50 per cent of their activity when boiled for 5 minutes at 100 C. Intramuscular injections are used in routine work, although either subcutaneous or intravenous methods may be used in special instances. Only 2 per cent of streptomycin is absorbed from the intestinal tract so that per oral administration of the drug is contraindicated when systemic effects are desired. The dosage necessary to maintain adequate blood levels varies somewhat in different individuals and both dosage and length of treatment, especially in tuberculosis, lack standardization.

Failure to clear the urine of simple infections by streptomycin within a week or two is attributed either to bacterial resistance or to mechanical factors such as stasis incident to obstructive uropathy, and the treatment in most instances is discontinued. The total dosage is small and toxic reactions relatively unimportant. The treatment of tuberculosis, on the contrary, is often started in ignorance of bacterial sensitivity and continued over prolonged periods of time without accurate means of determining asquired bacterial resistance in vivo. The total dosage is large and the danger of toxic reactions correspondingly greater. This therapeutic empiricism is unavoidable.

Keefer and his co-workers called attention to the desirability of maintaining concentrations of streptomycin in the blood 4 to 8 times that necessary to completely inhibit the growth of the organisms in vitro, because the presence of blood or serum may increase their tolerance to the antibiotic to this degree. It is questionable if levels of this degree could be maintained within the limits of safety.

In the Veterans Bureau report of August 1947, it is stated that all of 132 strains of the tubercle bacillus obtained from the sputum and urine of patients, prior to streptomycin therapy, were sensitive to concentrations of 3 micrograms of streptomycin per cubic centimeter in vitro, and the vast majority, to 1 microgram per cubic centimeter or even less. It is further stated that with the dosage of 1.8 to 2 gm. daily, concentrations of streptomycin in the circulating blood plasma does not fall below 5 micrograms per cubic centimeter so that at the outset of treatment therapeutically high blood levels are present. The dosage now advocated by the Veterans Bureau is 1 gm. daily and I am informed that reduction of the daily dosage to ½ gm. is under consideration. In vitro tests have disclosed acquired resistance of the organisms to streptomycin as treatment continues and it is reasonable to suppose that resistance in vitro means resistance in vivo, but it is impracticable as yet to take full advantage of this knowledge.

We have used either 1.8 or 2 gm. streptomycin daily in our cases of tuberculosis in divided doses at 3 hour intervals. The toxic reactions with the exception of slight vestibular reactions have been few. Attention may be called to a case in which severe anaphylactic reactions occurred after 4 days' treatment with combined penicillin and streptomycin. The reaction, which lasted 2 weeks, was characterized by fever, marked swelling of the face and extremities and large multiple wheals. In one of our cases, and in several reported instances, severe renal pain occurred, due apparently to local action of streptomycin, which is a renal irritant and may cause damage to the kidneys. Gross hematuria has not been observed while microscopic blood casts and albumin are not infrequently found. These are not serious unless there is increasing retention of blood urea nitrogen which would necessitate stoppage of treatment. Involvement of the auditory branch of the eighth nerve leading to permanent deafness is a rare but definite hazard. We have observed severe vertigo with diplopia.

PERSONAL EXPERIENCE

Of the 8 cases of urogenital tuberculosis treated with streptomycin under our observation, 3 present features of special interest.

In the first case, an acute tuberculous epididymal abscess developed during treatment. The second case is one of very early unilateral renal tuberculosis and possibly the only one of its kind thus far subjected to streptomycin therapy. The third case is representative of the results obtainable in most cases of ancient bilateral renal tuberculosis, in that the urine was promptly freed of tubercle bacilli, but this proved to be only temporary.

Case 1. A man aged 31 was first seen by us in 1930, when he complained of right flank pain and gross hematuria. The diagnosis of unilateral (right) renal tuberculosis was made and nephrectomy advised. The patient was not heard from again until 1939 when he returned for re-examination in anticipation of marriage. With the exception of slight frequency he was symptom free. Examination disclosed a well healed lesion in the region of the right ureteral orifice and a huge tuberculous pyonephrosis, on the right side. The left kidney was normal. The right kidney was removed. The patient remained in good health, having been married in the meantime. He was the father of 2 children, which is interesting in view of the extensive genital tuberculosis which was found later. The patient remained in good health until November 1946 when he returned complaining of pain in the left renal area and marked urinary frequency. Urograms disclosed dilatation of the left ureter but nothing suggestive of tuberculosis of the kidney. The epididymis, seminal vesicles, and prostate gland were extensively involved. Streptomycin therapy was started on March 1, 1947 and continued until April 15, 1947 in a dosage of 0.3 gm. every third hour with a total dosage of 125 gm. Urine cultures for the tubercle bacillus were positive on February 25, and thereafter 6 cultures were negative, the last one being taken May 24. Strangely enough during the course of the treatment the patient developed acute tuberculous epididymitis necessitating operation, which may have been due to acquired resistance of the tubercle bacillus to streptomycin. At the present time the patient is in good condition, having gained 16 pounds in weight and there is very little palpable evidence of involvement of the prostate gland and seminal vesicles. Urograms show some decrease of the dilatation of the left ureter. Cultures of the urine taken October 8, 1947 remain sterile but it was reported that acid fast bacilli were found in smears.

Case 2. Mrs. W. G. aged 35 was admitted to the Pennsylvania Hospital in May 1947 with a long history of pulmonary tuberculosis. Several years before admission she had had a spinal fusion for tuberculosis of the lumbar spine. Cystoscopic examination disclosed active vesical tuberculosis limited to the region of the right ureteral orifice. This was apparently of recent origin and without ulceration. Urographic study disclosed minor changes in the right renal pelvis and a normal pelvis on the left side. The urine contained an occasional red blood cell. The blood urea nitrogen was 16 mg. per cent, the phenolsulphonphthalein output 53 per cent. Cultures of urine from the bladder and right kidney were positive for the tubercle bacillus; the urine from the left kidney was sterile. Streptomycin (1.8 gm. daily for 78 days) with a total dosage of 140 gm. was given. The patient returned to the hospital on August 25, 1947 complaining of vertigo and severe pain in the right renal area. Cultures of urine from the right kidney were again positive and retrograde pyelography disclosed minor changes in the upper minor calyx highly suggestive of tuberculosis. On October 10 the patient was again admitted to the hospital complaining of very severe pain in the right kidney, frequency of urination and moderate hematuria. The blood urea nitrogen was now 19 mg. per cent and the phenolsulphonphthalein output 43 per cent. Differential studies showed 10 per cent output of phenolsulphonphthalein from the right kidney during a 15 minute period and 12.5 per cent from the left kidney. The kidney urines were sterile. On November 14, 1947 cystoscopic examination disclosed slight reddening around the right ureteral orifice. The urine from each kidney was sparkling clear. The right kidney excreted phenolsulphonphthalein in 3½ minutes and 12½ per cent in 15 minutes, the left kidney in 2½ minutes and 15 per cent in 15 minutes. The retrograde pyelogram we believe shows evidence of healing of the tuberculous lesion. Re-examination in October 1948 showed complete healing of the renal lesion and sterile urine. Her general health was excellent.

complicating lesions in the presence of tuberculosis. It is likewise his opinion that by reducing the number of tubercle bacilli through streptomycin therapy the powers of natural resistance may be increased. We are deeply indebted to those who kindly furnished the above data. Our limited personal experience together with interpretation of available data would seem to justify the following summary.

There is yet no justification for attempting final evaluation of streptomycin therapy on the basis of clinical experience.

Streptomycin exerts considerable bacteriostatic effect on tubercle bacilli resident in the human urogenital tract.

Total arrest of bacterial activity seems to occur in some cases of urogenital tuberculosis but this often proves to be temporary.

Streptomycin promotes the healing of tuberculous operative wounds and may prevent their occurrence.

Streptomycin is most effective in the treatment of early tuberculous lesions.

Tubercle bacilli embedded in chronic sclerosing and necrotizing lesions are probably not affected by blood borne agents such as streptomycin for mechanical reasons.

The probabilities are that the unilateral surgical tuberculous kidney should be removed in the absence of active pulmonary tuberculosis or other extrarenal complications. There is however neither clinical nor pathological evidence to deny the possibility of cure by streptomycin in very early cases.

There is the possibility that the preoperative use of streptomycin in apparently unilateral renal infections may decrease the incidence of active tuberculosis in the supposedly healthy kidney after operation.

If streptomycin is used pre-operatively the possibility of injury to the apparently healthy kidney must be kept in mind.

Medical Arts Bldg., Philadelphia 2, Pa.

REFERENCES

Buggs, C. W., Bronstein, B., Hirschfeld, J. W. and Pilling, M. A.: J. A. M. A., 130: 64–67, 1946.
Cook, E. N., Greene, L. F. and Hinshaw, H. C.: Proc. Staff Meet., Mayo Clin., 21: 277, 1946.
Farrington, R. F., Hull-Smith, H., Bunn, P. A. and McDermott, W.: J. A. M. A., 134: 679–688, 1947.
Hinshaw, H. C. and Feldman, W. H.: Proc. Staff Meet., Mayo Clin., 20: 313–318, 1945.
Huffines, T.: Personal communication.
Keefer, C. S., et al.: J. A. M. A., 132: 4–11 and 70–77, 1946.
Mathé, C. P.: J. Urol., 57: 451–459, 1947.
——: Urol. & Cutan. Rev., 51: 305–307, 1947.
McDermott, W.: Am. J. Med., 2: 491–501, 1947.
Olsen, A. M.: Proc. Staff Meet., Mayo Clin., 21: 53, 1946.
Redewell, F. H.: J. Urol., 58: 35–46, 1947.
Schatz, A., Bugie, E., and Waksman, S. A.: Proc. Soc. Exper. Biol. and Med., 55: 66–99, 1944.
Schatz, A., and Waksman, S. A.: Proc. Soc. Exper. Biol. and Med., 55: 244, 1944.
Slotkin, G. E.: Personal communication.
Thomas, G. J.: Personal communication.
Veterans Administration Tech. Bull., 10–34, Aug. 5, 1947; and 10–37, Sept. 24, 1947.
Smith, N. and McCloskey, W. T.: Public Health Reports, 60: 1129–1138, 1945.
Youmans, G. P. and McCarter, J. C.: Am. Rev. Tuberculosis, 54: 432–439, 1945.

THE JOURNAL OF UROLOGY
Vol. 61, No. 1, January 1949
Printed in U.S.A.

THE INCREASED PATHOGENICITY OF BACILLUS LACTIS AEROGENES IN URINARY TRACT INFECTIONS[1]

SEYMOUR F. WILHELM AND LAZARUS A. ORKIN

From the Genito-Urinary Surgical Service, Beth Israel Hospital, New York, N. Y.

A remarkable change has recently been observed in the bacterial flora urinary tract infection. *Especially striking is the decided increase in t* frequency of B. lactis aerogenes (Aerobacter aerogenes) and B. pyocyane (Pseudomonas aeruginosa).

This report is confined solely to a consideration of B. lactis aerogenes sir an excellent study of Pseudomonas aeruginosa was published by Carroll a his co-workers last year. Although the clinical impression recently obtain is that B. lactis aerogenes is more prevalent in the urinary tract, there is no lar statistical review available which bears out this contention.

An analysis was, therefore, made of 211 consecutive admissions to the Genit Urinary Surgical Service of the Beth Israel Hospital in 1940 and 1941, and con pared to a similar analysis of 350 consecutive admissions between 1945 and 19 (fig. 1). In 1940–41, B. lactis aerogenes was recovered either in pure or mixed culture from the urine in 6.6 per cent of the admissions, as contrasted 45.7 per cent in 1945–48. The total admissions represent a lesser number patients, since some entered the hospital more than once. Calculated on t basis of patient number, the incidence of B. lactis aerogenes proved appro imately the same. *Thus, during 1940–41, there were 12 instances of B. lact* aerogenes in 163 patients (7.4 %), as compared to 1945–48, when there we 126 instances in 257 patients (49.2 per cent) (fig. 2).

B. lactis aerogenes must be distinguished from B. coli which it resembl closely. When a urine sample is submitted for culture in our laboratory, direct smear is made of the urinary sediment. One drop is streaked on a bloc agar plate, 1 drop on Chapman's plate, and 1 drop is put in glucose broth. A the end of 24 hours' incubation at 37 degrees C., the plates are read, and smea made of the organisms that have been grown out. If, however, there has bee no growth on the plates and gram negative organisms are found in the brot another subculture is made on Chapman's plate.

E. Seligmann has found the use of Chapman's plate most satisfactory. O this medium, B. lactis aerogenes produces greenish yellow gumdrop colonie which are surrounded by yellow zones. These colonies are much larger tha the flat colonies of B. coli, which are yellow surrounded also by yellow zones.

PATHOGENICITY

Having established a tremendously increased incidence of B. lactis aerogenes i recent years, we were next concerned with the pathogenicity of this organis Formerly, it was believed that B. lactis aerogenes was, for the most part, non

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 1 1948.

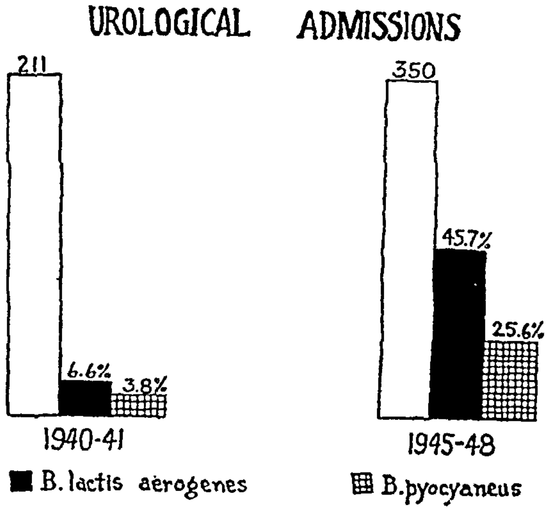


FIG. 1

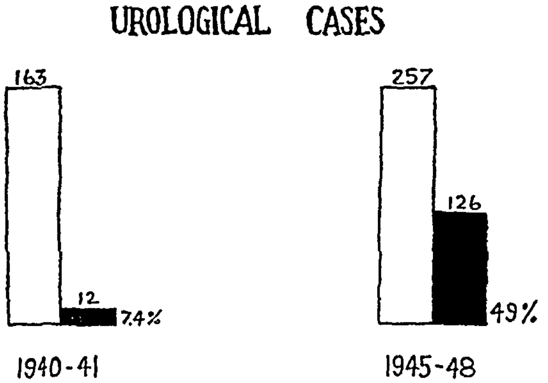


FIG. 2

TABLE 1. *B. lactis aerogenes bacteremia with urinary infection*

B. I. H. CASE NO.	SEX	DIAGNOSIS	RESISTANCE TO STREPTOMYCIN		DOSAGE STREPTOMYCIN	SUBSEQUENT URINE CULTURE	FOLLOW-UP URINE CULTURE	RESULT
			1st culture					
			Urine	Blood				
191213	M	Hyper. prostate; postprostatectomy	Over 64 units	Over 64 units	3 gm. 5 days	Over 64 units	Died	Died
190556 195535	M	Renal calculi; pyelonephritis	Over 32 units	Over 32 units	2 gm. 7 days	Over 32 units	B. lactis aerogenes over 32	B. aerogenes infection persisted over 10 months
194323	M	Hyper. prostate; postprostatectomy	Over 64 units	Over 64 units	3 gm. 4 days	Over 64 units	No growth 11 months later	Cured
201045	F	Urinary retention; diabetic tabes	Over 64 units	Over 64 units	2 gm. 6 days	Over 64 units	B. lactis aerogenes	B. lactis aerogenes infection persisted 3 mos.

pathogenic, although isolated cases of severe and, at times, fatal infection with pure culture of B. lactis aerogenes have been reported. In 1929, Hill and her associates studied 200 cultures of gram negative bacilli from the urinary tract and found 79 instances (39.5 per cent) of B. lactis aerogenes. More recently, Herrell and Nichols found 3 cases of Aerobacter aerogenes among 13 urinary infections, and Adcock and Plumb found 5 cases among 11.

In the authors' 12 cases of 1940–41, there were no fatalities, nor were there any with a positive blood culture. On the other hand, in the 126 cases from 1945–48, there were 4 who were gravely ill with positive blood cultures of B. lactis aerogenes; one of these patients died (table 1).

BACTEREMIA: CASE REPORTS

Case 17. (Beth Israel Hospital No. 191213.) Suprapubic prostatectomy for benign hypertrophy, B. lactis aerogenes bacteremia; died. A 62 year old man entered the hospital on February 8, 1947, because of prolonged urinary retention. The urine was grossly infected and culture showed B. proteus and coliform organisms. The blood nonprotein nitrogen was 100 mg. per cent, and despite catheter drainage rose to 128 mg. per cent.

On February 12, a suprapubic cystostomy was done. One hundred twenty thousand units of penicillin were administered daily for the next week, following which the patient received 9 gm. of sulfadiazine in 6 days. Low-grade fever persisted, and mandelamine, sulfamerazine, NU 445-9, and penicillin, in turn, were administered.

Urine culture of February 24 and March 11 again revealed B. proteus and coliform organisms. However, on March 14, 15, and 18, B. lactis aerogenes was found. On March 20 and 31, urine culture showed both B. lactis aerogenes and enterococci.

On April 1, eleven weeks after the cystostomy, the enlarged prostate was enucleated suprapubically. Two days later, packings were removed from the prostatic bed with strict asepsis. A Foley catheter was inserted transurethrally and removed the following day. Four hundred thousand units of penicillin were administered daily. The temperature ranged between 102 and 103 F. for the next 3 days, and on April 6, there was a severe chill and rise of temperature to 106 F. At this time, there was evidence of pulmonary consolidation in the right lower lobe and both a urine culture and a blood culture showed B. lactis aerogenes resistant to more than 64 units of streptomycin.

Despite the resistance of the organism, 3 gm. streptomycin were given daily in divided doses, in addition to intravenous sodium sulfadiazine. On April 8, the patient's condition was poor and the temperature went to 105.8 F. Blood cultures on April 8, 9, and 10, showed innumerable colonies of B. lactis aerogenes, resistant to more than 64 units of streptomycin.

With persistent bacteremia, the likelihood of septic periprostatic thrombophlebitis was considered, and ligation of the inferior vena cava proposed. Before this could be done, the patient suffered a severe bladder hemorrhage, which was controlled by packing and blood transfusion. Frequent chills continued and the *urinary output declined.* On April 11, streptomycin was discontinued, 15 gm. having been administered in 5 days. The patient died in anuria and coma on April 14, the thirteenth postoperative day. Autopsy was refused.

Case 24. (*Beth Israel Hospital No. 190556 and No. 195535.*) *Renal calculus and bilateral ureteral calculi; suppurative pyelonephritis; B. lactis aerogenes bacteremia; nephrectomy; recovered.* A 63 year old man entered the hospital on January 18, 1947, complaining of pain in both loins and blood urine of 3 weeks' duration. He had suffered from bilateral renal colic and hematuria for 10 years.

The urine was loaded with white blood cells and culture showed B. proteus and coliform organisms. Simple film and excretory urography revealed a dendritic calculus in the right renal pelvis and a smaller calculus in the right upper ureter with moderate hydronephrosis. On the left side, there was a large lower ureteral calculus with a dilated double ureter and hydronephrosis. Another urine culture showed B. proteus.

On January 21, a low left ureterolithotomy was performed. The wound healed by primary intention, but the patient continued to run a septic course with temperature up to 102.4 F. This was attributed to right pyelonephritis, although excretory urography revealed good function on both sides. On January 28, the patient began to receive 30,000 units of penicillin every 3 hours, to which was added, several days later, 0.5 gm. sulfadiazine, 3 times daily. Urine culture now revealed B. lactis aerogenes.

The fever persisted and, on February 8, the temperature was elevated to 105.4 degrees. A blood culture was sterile. Two days later, there was definite evidence of a right lower lobe pneumonia. Urine culture on this date again showed B. lactis aerogenes, resistant to more than 32 units of streptomycin. A second blood culture revealed no growth. The pneumonic process gradually cleared up, the temperature returning to normal by March 8. Urine cultures on February 14 and 25, and on March 11, showed B. lactis aerogenes.

On March 8, a right pyelolithotomy and ureterolithotomy were done. Penicillin was again administered, with daily dosage of 240,000 units. The temperature was elevated between 100 and 102 F., and on the fourth postoperative day the wound, which became grossly infected, was opened widely. Culture of the wound pus revealed B. lactis aerogenes, resistant to more than 32 units of streptomycin. Since the fever persisted despite adequate wound drainage, it was felt that a suppurative infection of the right renal cortex was present. Two grams of streptomycin and 800,000 units of penicillin were administered daily beginning March 13. However, the patient experienced another chill on March 17 with temperature of 105.8 F. Blood culture was postive for B. lactis aerogenes.

On March 18, a right nephrectomy was done. The patient pursued a low-grade febrile course until March 22. A blood culture on March 21 revealed B. lactis aerogenes, but all the subsequent blood cultures showed no growth. The patient improved consistently and left the hospital on April 17, with frank pyuria and the urine still containing B. lactis aerogenes.

The patient returned to the hospital on June 14, 1947, for plastic revision of the nephrectomy wound. On that day and on June 23, urine culture revealed B. lactis aerogenes. The patient left the hospital on June 28, and at follow-up on April 3, 1948, he still had marked pyuria. Urine culture showed B. lactis aerogenes, resistant to more than 64 units of streptomycin.

Case 36. (Beth Israel Hospital No. 194323.) Prostatectomy for benign hypertrophy; late hemorrhage, B. lactis aerogenes bacteremia; recovery. A 63 year old man was admitted to the hospital on May 11, 1947, with symptoms of prostatism. The urine showed from 5 to 8 white blood cells per high power field and culture revealed Staphylococcus albus. A suprapubic prostatectomy was done on May 13, and 2 days later gauze packings were removed with strict asepsis. For the first 2 postoperative days, 50,000 units of penicillin were administered every 3 hours. Following this, 2 gm. of sulfadiazine were given daily.

The course was uneventful until the sixteenth postoperative day when the patient suddenly suffered a brisk hemorrhage from his bladder. Blood clots were evacuated and the bleeding controlled by a Foley catheter. Eight hundred thousand units of penicillin were administered daily. Shortly thereafter, the patient had a severe chill with temperature of 105.8 F. Blood culture showed many colonies of B. lactis aerogenes resistant to more than 64 units of streptomycin; urine culture showed B. pyocyaneus and B. lactis aerogenes also resistant to more than 64 units. It was felt that the patient was suffering from a septic periprostatic phlebitis. On June 2, both the blood culture and the urine culture were again positive for B. lactis aerogenes. On June 3, however, blood culture was sterile; urine culture showed B. lactis aerogenes.

Three grams of streptomycin were given daily in divided doses for 4 days. Between May 31 and June 4, the temperature was elevated daily to 104 and 105 degrees, but on June 5, the temperature became low-grade and, shortly thereafter, normal. From June 8, 2 gm. of sulfadiazine were administered daily. Urine culture remained positive for B. lactis aerogenes.

The patient left the hospital on June 20 with a healed wound and voiding well. However, pyuria persisted and culture was still positive for B. lactis aerogenes. When last examined on April 8, 1948, the patient was completely well and urine culture showed no growth.

Case 70. (Beth Israel Hospital No. 160980 and No. 201045.) Neurogenic bladder; diabetic tabes with B. lactis aerogenes cystitis, pyelonephritis, and bacteremia; recovered. A 55 year old woman, a known diabetic, was admitted to the hospital on December 6, 1947, complaining of difficulty in starting the urinary stream and inability to empty the bladder. Her symptoms were of 5 years' duration and, on a previous hospital admission, a transurethral resection had been done. For a short time thereafter, the patient voided fairly well, but gradually the symptoms recurred. There were now over 500 cc. of purulent residual urine, culture of which revealed B. lactis aerogenes.

Two grams of sulfadiazine were administered daily and, on December 9, an anterior colporraphy and suspension of the urethra were done by a gynecologist. After the operation, the patient was given 3 tablets of mandelamine, 4 times daily. The urethral catheter was removed on the eighth postoperative day, but the patient was unable to void. The catheter was replaced, tidal drainage was instituted, and 50,000 units of penicillin administered every 3 hours. Urine culture showed B. lactis aerogenes resistant to 64 units of streptomycin. On December 24, the patient experienced 3 chills, accompanied by temperature elevation to 105 F. and severe left loin pain. Blood culture and urine culture revealed B. lactis aerogenes; in each, the organism was resistant to more than 64 units of streptomycin. On December 25, blood culture grew out 115 colonies of B. lactis aerogenes per cubic centimeter. Two grams of streptomycin were administered daily and the temperature gradually came down to 100 degrees on December 30, and was normal thereafter. Streptomycin was discontinued on December 28, and a urine culture on December 30 showed B. lactis aerogenes.

The patient was able to void in small amounts, but, at the time of discharge from the hospital, there was a residual urine of from 150 to 250 cc which has persisted. Urine culture on discharge showed B. lactis aerogenes and was still positive on April 8, four months later.

COMMENT

Practically all of the 126 patients in the 1945–48 series presented symptoms and signs of urinary tract infection. In many, B. lactis aerogenes was recovered in pure culture directly from the infected organ at operation, from the excised surgical specimen, or, postoperatively, from infected wounds. These clinical observations, combined with the 4 above reported cases of bacteremia, each with repeated blood cultures showing a pure growth of B. lactis aerogenes, have convinced us that this organism, when present in the urinary tract, is now usually pathogenic and may give rise to serious and sometimes fatal infection.

STREPTOMYCIN SENSITIVITY

Most reports in the literature (Helmholz; Herrell and Nichols; Kleinman, Shearer and Sprinz) emphasize the sensitivity of B. lactis aerogenes to streptomycin, as well as the practical effectiveness of this drug in these urinary infections. Pulaski in a study of 29 Aerobacter aerogenes infections discovered that the great majority were sensitive to 16 units or less. In only 2 cases were resistant organisms encountered. Buggs and his co-workers found susceptibility to streptomycin in 17 out of the 20 strains studied. Adcock and Plumb reported sensitivity to from 0.8 to 1.5 units in his 5 cases of B. lactis aerogenes, and he, as well as Pool and Cook, were able to eradicate the infections promptly with streptomycin in all cases.

In the authors' 1945–48 series, the streptomycin sensitivity of B. lactis aerogenes was determined on initial culture in 104 cases (table 2). Ninety-one (88 per cent) were found resistant, i.e., not inhibited by more than 16 units. These figures roughly agree with those compiled by our bacteriologist, E. Seligmann, from 196 patients with B. lactis aerogenes infection from the entire hospital. Of these, 163 (82.3 per cent) proved resistant on initial culture. It is of interest that of 48 ambulatory patients from the Out-Patient Department, only 23 (47.9 per cent) were found resistant, suggesting that at least some of the in-patients may have been infected after admission by a resistant strain indigenous to the hospital. Supporting this assumption is the fact that, on admission to the hospital, only 61 of 126 cultures (48 per cent) showed B. lactis aerogenes, while in 126 subsequent cultures this organism was recovered in 111 (92 per cent).

Streptomycin sensitivity tests were done on subsequent cultures in 44 cases (table 3). In 42 of these, the sensitivity remained the same; in one it decreased, and in the remaining one it increased.

Streptomycin sensitivity was determined by a serial dilution method, with a B. coli as test strain.

TABLE 2 *Sensitivity to streptomycin on initial culture*

	CASES
Over 64 units	60
Over 32 units	27
Over 16 units	4
8 units	1
4 units	5
2 units	2
1 unit	2
½ unit	3
Total cultures	104
Over 16 units	91 (88%)
Under 16 units	13 (12%)

TABLE 3 *Streptomycin sensitivity on repeated cultures*

Total cases	44
No change in sensitivity	42
Sensitivity increased (8 to 64 units)	1
Sensitivity decreased (64 to ½ unit)	1

Our observations show a very high incidence of resistance to streptomycin on initial culture, and a remarkable constancy of this characteristic of B lactis aerogenes.

TREATMENT WITH STREPTOMYCIN

Thirty-two of the 126 cases were treated with streptomycin. Three of these were sensitive to less than 16 units on initial culture; 1 was cured, but the other 2 persisted. In the latter 2, the organism became resistant to over 64 units on subsequent cultures.

Twenty-six cases, resistant to over 16 units on initial culture, were treated with streptomycin. Three cleared up. Three additional cases, in which no sensitivity determination was made, cleared up with streptomycin.

Of the 32 patients with B. lactis aerogenes urinary infection treated with streptomycin, 7 cleared up and 21 persisted. There was no follow-up in 4.

These results suggest that the usefulness of streptomycin alone is sharply limited and that other additional therapeutic means must be sought in the treatment of B. lactis aerogenes urinary infection.

RESULTS

The 12 patients seen in 1940–41 were followed with subsequent cultures. In all of these, B. lactis aerogenes disappeared in from 6 months to 7 years.

Ninety-three of the 126 cases of the 1945–48 series were followed. In 68 (73 per cent) the infection persisted, and in 25 cleared up (27 per cent) (table 4). Since streptomycin was administered to only 7 of these patients, it is apparent that the cure in most cases was not the result of specific treatment. Persistent B. lactis aerogenes urinary infection was treated with a variety of drugs, such as penicillin, sulfadiazine, NU 445–9, mandelamine, singly and in combination, in practically all instances. These clinical observations indicate that B. lactis aerogenes urinary infection is in large measure not susceptible to the commonly used present-day therapeutic agents.

TABLE 4. *Cases of B. lactis aerogenes: 1945–48*

Total number	126
Cases followed	93
Infection persisted	68–73%
Infection cleared up	25–27%
Died	8

SUMMARY

A striking increase in the frequency of B. lactis aerogenes urinary infection has been observed. An analysis of 2 series of consecutive cases reveals that the incidence has risen from 7.3 per cent in 1940–41 to 49.2 per cent in 1945–48.

Clinical observations indicate that B. lactis aerogenes is now usually pathogenic and often gives rise to serious and sometimes fatal infection. Four cases of bacteremia, each with repeated positive blood cultures showing a pure growth of B. lactis aerogenes, are reported in detail.

Streptomycin sensitivity of B. lactis aerogenes was determined on initial culture in 104 cases. Contrary to most previous reports, 88 per cent were found resistant to more than 16 units.

Streptomycin sensitivity tests on 44 subsequent cultures showed remarkable constancy of this characteristic of B. lactis aerogenes.

Thirty-two patients were treated with streptomycin; 7 cleared up and 21 persisted. The usefulness of streptomycin alone is sharply limited in the treatment of B. lactis aerogenes urinary infection.

Ninety-three cases were followed with repeated cultures. In 73 per cent, the infection persisted. In the 25 cases which cleared up, the cure, for the most part, was not the result of any specific treatment. B. lactis aerogenes urinary infection is, in large measure, not susceptible to the commonly used therapeutic agents.

Antibiotics, as well as sulfa drugs, should therefore be selectively administered only to patients whose urine cultures reveal susceptible organisms. By following this rule, a considerable reduction in undesirable and, at times, dangerous allergic reactions will be effected, as well as a large saving in cost.

The authors wish to express their appreciation to Dr. Erich Seligmann for his assistance and helpful suggestions.

40 E. 83rd St., New York, N. Y.
150 E. 73rd. St., New York, NY

REFERENCES

Adcock, J. D. and Plumb, R. T.: J.A.M.A., 133: 579, 1947.
Buggs, C. W., Bronstein, B., Hirshfeld, J. W. and Pilling, M. A.: J.A.M.A., 130: 64, 1946.
Carroll, G., Allen, H. N. and Doubly, E. R.: J.A.M.A., 135: 683, 1947.
Chapman, G. H.: J. Bact., 53: 504, 1947.
Helmholz, H. F.: Proc. Staff Meet., Mayo Clinic, 20: 357, 1945.
Herrell, W. E. and Nichols, D. R.: Proc. Staff Meet., Mayo Clinic, 20: 449, 1945.
Hill, J. H., Seidman, L. R., Stadnichenko, A. M. S. and Ellis, M. G.: J. Bact., 17: 203, 1929.
Kleinman, A. M., Shearer, T. P. and Sprinz, H.: J. Urol., 57: 599, 1947.
Pool, T. L. and Cook, E. N.: J.A.M.A., 133: 584, 1947.
Pulaski, E. J.: Ann. Surg., 124: 392, 1946.
Seligmann, E. Personal communication.

The Journal of Urology
Vol. 61, No. 1, January 1949
Printed in U.S.A.

DISCUSSION

Dr. Grayson Carroll (St. Louis, Mo.): This presentation which demonstrates the increased prevalence and pathogenicity of the Aerobacter aerogenes is quite timely.

In a series of cultures taken on our St. Louis City Hospital Service, in 1947, Dr. Reagen, the resident urologist, gives me the following report, indicating the prevalence of various organisms found. You will note that the Aerobacter aerogenes appeared in 35 patients out of a total of 481 patients examined, giving a percentage of 7.5.

Escherichia coli	128	26.6%
Pseudomonas aeruginosa	72	10.0%
Paracolon	49	
Micrococcus	55	
Aerobacter aerogenes	35	7.5%
Staphylococcus albus	16	8.0%
Hemolytic staphylococcus albus	10	
Hemolytic staphylococcus aureus	6	
Staphylococcus aureus	8	
Undifferentiated streptococcus	20	8.0%
Gamma streptococcus	10	
Beta streptococcus	10	
Alpha streptococcus	8	
Alkaligenes faecalis	11	
Klebsiella	1	
Diphtheroids	15	
Intracellular gram neg. diplococci	2	
Proteus vulgaris	21	4.0%
Yeast	4	
	481	

In a study of 200 patients in our private practice, 10 patients had Aerobacter aerogenes as an infecting organism or 5 per cent. The list of organisms and the relative prevalence in this series is as follows:

Escherichia coli	104	50.0%
Staphylococcus aureus	28	
Mixed staphylococcus and Escherichia coli	23	
Staphylococcus albus	5	
Streptococcus	8	
Aerobacter aerogenes	10	5.0%
B. proteus	5	
No growth	9	
Gram-positive	6	
Streptothrix	1	
Pleomorphic streptococcus	1	
	200	

This compares rather favorably with the series noted in the essayist's presentation in the years 1940–41, which was 7.3 per cent.

I am inclined to think that the 49 per cent noted in the years 1945 to 1948 is high for clinics over the country. But that these organisms are on the increase, I quite agree, due no doubt to its resistance to antibiotics and other drug inhibitors. The Escherichia coli being repressed, the Aerobacter becomes the dominant strain. This is demonstrated in Dr. Wilhelm's experience. Other organisms were cultured on admission but later the Aerobacter became the organism surviving to prolong the illness.

We strongly advocate, as does the essayist, the use of culture and identification of the organism and—sensitivity tests made in the laboratory on all resistant cases and avoid the expensive and some times hazardous, prolonged administration of drugs.

We had a patient treated for 2 weeks with 3-hour injections of streptomycin only to find that the particular strain of Pseudomonas involved could not be inhibited with 50 micro-units of streptomycin.

Sensitivity tests were carried out in our laboratory on the B. lactis aerogenes received from Dr. Wilhelm's service in New York City. These tests were made, not only with streptomycin, but, also, with penicillin, mandelic acid and sodium sulfadiazine. The results are, herewith, tabulated:

c̄	Streptomycin (u.)	100	50	10	5	.5	.1	Cont.	
		+	+	+	+	+	+	+	
c̄	Penicillin (u.)	500	100	50	25	.10	.5	.5	Cont.
		−	+	+	+	+	+	+	+
c̄	Mandelic acid (pH 5.5–6) (%)	1	.5	0.25	0.125		Cont.	Cont.	
		−	−	−	−		+		
c̄	Sodium sulfadiazine (mg.)	125	50	25	10	5	1	0.5	Cont.
		−	−	+	+	+	+	+	+

It will be seen that the streptomycin was totally ineffective against this strain in up to 100 units which obviously is impossible to produce in a clinical case. Likewise, more than 100 units of penicillin were required to cause inhibition, which again makes it impractical for clinical use.

The mandelic acid, however, in all instances, even in the concentration of 0.1 per cent, caused inhibition.

With the sodium sulfadiazine, 25 mg. were required, which obviously is high.

A strain of Aerobacter aerogenes, isolated from the urine of a patient at our St. Louis City Hospital, was also subjected to sensitivity tests with the tabulated results:

c̄	Streptomycin (u.)	100	50	25	10	5	1	0.5	0.1	Cont.
		+	+	+	+	+	+	+	+	+
c̄	Penicillin (u.)	500	100	50	25	10	5	0.5	0.1	Cont.
		+	+	+	+	+	+	+	+	+
c̄	Mandelic acid (%)	1	.5	0.25	1.125	Cont.				
		−	−	−	−	+				
c̄	Sodium sulfadiazine (mg.)	125	50	25	10	5	1	0.5	Cont.	
		−	−	+	+	+	+	+	+	

It is to be noted that here again the streptomycin, penicillin and sodium sulfadiazine were ineffective and only the mandelic acid in very low concentration caused inhibition when the pH was 5.5.

It is not necessarily to be construed, however, that all patients with Aerobacter aerogenes will be cured with the administration of mandelic acid, since the drug is not blood-borne, but is contained in the urine excreted. When mandelic acid has been poorly tolerated by mouth, we have used 20 per cent sodium mandelate administered intravenously.

It is apparent that there are more and more bacilliary strains that are highly resistant to practically all of our known antibiotics and as time goes on, these surviving strains will, undoubtedly, constitute a higher percentage of urinary infections as the more susceptible strains are destroyed. It is evident that asepsis must be diligently practiced when it is realized that such an infection, carried to another patient, is so difficult to successfully treat and is so pathogenic. We are again in need of a new weapon to fight these surviving bacteria.

DR. LAZARUS A. ORKIN (New York, N. Y.): Bacillus lactis aerogenes, a gram negative organism, must be differentiated from B. coli, which it so closely resembles. Although it is nonmobile, is shorter, and plumper than B. coli, the morphological differences are minor and variable, and cannot be used for differentiation. Many tests and criteria have been used, but the best method is by the use of Chapman's plate.

On this medium there is no inhibition of the coliform organisms, thus permitting recovery from minute inocula, and the bacterial counts are said to be 30 per cent higher than on other selective media.

Since no other bacteria are said to grow on this plate, and since B. lactis grows luxuriantly, it serves as an excellent means of quickly differentiating aerogenes from other organisms, more especially B. coli. It is less time-consuming and more selective. B. coli produces flat yellow colonies surrounded by yellow zones; B. lactis produces large greenish-yellow gumdrop colonies surrounded by a yellow zone.

From our recent experience we can definitely say that if more laboratories would be more painstaking in the differentiation between these two organisms, more cases of Aerobacter aerogenes infection would be unearthed.

The fact that bacteria may develop resistance or tolerance to various chemotherapeutic substances is now well recognized. It is suggested that the striking increase in Aerobacter aerogenes and other resistant bacteria, coincident with the widespread use of sulfa drugs and antibiotics, may be the result of a selective process. The resistant organisms have survived and flourished after the elimination of the susceptible organisms. The routine prophylactic use of sulfa drugs or antibiotics appears irrational, since the majority of the urinary tract infections in the 1945–48 series were caused by resistant organisms.

In accordance with the results in our study, we can definitely say that we now have a serious problem in urology, namely, the treatment of Aerobacter aerogenes infection, since the greater majority of these cases are resistant to our present chemotherapeutic agents.

Cultures are essential in all cases of urinary tract infections both on initial examination and at subsequent intervals. Sensitivity tests are a requisite guide in the administration of streptomycin. Sulfa drugs and antibiotics should, as a rule, not be used where complicating factors exist, as the presence of catheters and tubes, residual urine, persistent fistulas, urinary obstruction, and the presence of calculi. It is much better to wait until these are cleared up or removed.

Sulfa drugs and antibiotics should finally be selectively administered to patients whose urine cultures reveal susceptible organisms. By following these rules, the possibility of development of resistance of the organism is lessened, a considerable reduction in undesirable and at times dangerous allergic reactions will be effected, as well as a large saving in cost.

amputated clitoris measured 8 by 2 cm. and showed microscopically normal corpora cavernosa.

Androgenic hormone determinations were done on the urine, and it is noted on the hospital record that there was no difference in the androgenic titer between a preoperative specimen and one obtained 4½ months postoperatively.

The patient was not seen again until August 1947, when she came to the hospital to see if anything could be done to develop female secondary sex characteristics. Physical examination showed that there had been no change. She still had had no menstrual bleeding but had had a few lower abdominal cramps at rare intervals. The hair distribution and growth were as before. The breasts were perfectly flat without palpable glandular tissue. The patient had been married several years previously, and although she stated that her sex life was essentially normal, there had been no pregnancies. She was completely satisfied with the results of the operation in that removal of the enlarged clitoris had made her feel that she was now definitely a female and was no longer a "freak." She stated that there had never been any erotic sensations derived from her enlarged clitoris, so that its absence had had no effect on her sexual life.

Esther B., New Haven Hospital Unit No. B 93002, 42 years of age, was first seen February 11, 1947. The patient weighed 1½ pounds at birth but managed to survive. She didn't talk until the age of 8 years. At the age of 12 she was taken to a hospital to see what could be done about a "birth mark" (enlarged clitoris); however, nothing was done. At the age of 11–12 she had breasts "the size of hen's eggs." They then regressed and have been perfectly flat since then in spite of all sorts of nostrums which she has applied locally. She started shaving with her father's straight razor at the age of 9–10 years, beginning on her lower lip and gradually extending to the chin and upper lip. She had never had extensive hair growth on the cheeks but did have to shave a number of heavy black hairs in those regions. She started shaving her legs at the age of 13 years because of a heavy growth of dark hair and has similarly shaved her arms. At the age of 13 she started having cramps in her lower abdomen every month. She has never had menstrual bleeding and continues to have cramps now at the age of 42. The attacks of cramps have come at regular intervals occurring between the twentieth and thirtieth day of each month and lasting for 2 days. She has had a successful sex life stating that she has always been "pretty high-natured." She was married at the age of 15 years (1921) for the first time. The husband lived until 1928, when he died of Bright's disease. In 1929 she remarried, but the second husband ran off with another woman in 1945. She still has great libido which she "holds down" to some extent. She has always been satisfied at intercourse with the act being done in the usual manner. She stated that there was no sensation in her enlarged clitoris and that it had nothing to do with satisfaction at intercourse. Nothing of interest was revealed in her past history other than that she was a luetic and had received antiluetic treatment.

Physical examination:—Temperature, 98; pulse, 80; respirations, 16; blood pressure, 120/90. The patient was a short woman, 4 feet 9 inches, 42 years of age, with a rather raw-boned build. Her face appeared to be definitely masculine with rather rugged features. She had recently shaved her face, but there was heavy black stubble over the chin, lower and upper lips and sides of the mouth and over the cheeks. The hair of the head was thick, black, rather coarse and streaked with gray. Her shoulders and chest were squarely built and seemed to be as wide as her hips. She had masculine distribution of hair on the chest, around the nipples of the breasts, and over the abdomen and pubis. There was also rather heavy black hair over the legs. There was nothing remarkable about the formation of the extremities except that the muscles of her arms were very well developed, perhaps more than is usually noted in the biceps. Her skin was coarse and heavy, such as one sees in men. Moderate pigmentation, evenly distributed, was noted. The breasts were perfectly flat with no palpable glandular tissue. The nipples and areolae were not remarkable in formation other than being masculine in character. The abdomen showed nothing remarkable. There were no palpable masses other than the liver, which could be felt on deep inspiration. The abdomen was protuberant and lordosis of the spine was noted when the patient stood.

Pelvic examination:—There was a heavy growth of pubic hair. The labia majora and minora seemed to be essentially normal except that the top of each labium minorum extended up under and along the ventral surface of a very large clitoris to the ventral surface of the glans which was notched in the midline on its ventral surface where the labia met. There was a small amount of redundant foreskin around the lateral and superior margins of the glans; this was adherent to the sulcus of the corona on the dorsal aspect. The clitoris was about 2.5 to 3 cm. long and slightly more than 1 cm. in diameter. It was covered by normal skin, as on the labia, except that on its ventral aspect between the labia it had the pink color and smooth texture of the skin usually seen between the labia. On palpation it was soft and pliable. The glans did not appear remarkable; there was no urethral dimple. The urethra was in normal position for the female and appeared normal. The vagina admitted 2 fingers with ease and was in normal position with a normal vaginal mucosa. The pelvic floor appeared to be normal. The cervix, although one-half normal size, was smooth, round, firm, and freely mobile without pain, and had a normal configuration. The uterus was small, being about one-half normal size, anterior in position and freely mobile without pain. The adnexae were free of palpable masses and showed no tenderness.

Laboratory findings:—Red blood count, white blood count, hemoglobin, urine, nonprotein nitrogen and phthalein were normal. Mazzini, 2 plus. Spinal fluid Wassermann was negative.

Preoperative course:—Intravenous pyelograms showed completely normal outlines of both upper urinary tracts. Roentgenograms of the skull were normal. For analyses of two 24 hour collections of urine, see figure 1, for 17-ketosteroid, estrogenic and FSH determinations.

Operation:—Exploratory laparotomy and amputation of the clitoris were done. Both kidneys were palpated and found to be normal in size, shape and consistency. Both adrenals could be palpated just above the upper poles of the kidneys. They seemed to be normal in size, shape and consistency. They could not be exposed for examination or biopsy through the incision in the lower abdomen. The uterus was found to be of normal shape but small in size. It was approximately 6 cm. long and 4 cm. wide at its fundus. Two essentially normal-appearing fallopian tubes emerged from the uterus in a normal fashion. They led to the ovaries which were enveloped in many dense adhesions. There were many adhesions around the fimbriated ends of the fallopian tubes; these adhesions were divided so as to expose the ovaries. They appeared to be about normal in size, being about 2 cm. in diameter, and contained several small cysts about 2 mm. in diameter. A biopsy specimen 1 cm. wide and ½ cm. thick was removed from the central portion of each ovary.

Postoperative course:—A daily oral dose of 10 mg. stilbestrol was started on the patient's fourth postoperative day and was well tolerated. Her 17-ketosteroid excretion was determined. Preoperatively the readings ranged between 65.7 and 86.8 mg. per 24 hours. The normal level for females of her age group is 8, plus-minus 3. The level rose sharply during the second and third postoperative days, which is a normal occurrence. After the stilbestrol was started her 17-ketosteroid excretion level came down sharply, so that after 9 days of therapy about half the preoperative excretion level was obtained. She was discharged on her thirteenth postoperative day with well-healed wounds.

Pathology:—The amputated clitoris measured 8 cm. in length and 2 cm. in thickness. Skin covered only the distal 3 cm. of the specimen. On cross section two normal-appearing corpora cavernosa were seen. There was no visible corpus spongiosum. Microscopically the sections of the shaft of the clitoris showed the structures of normal corpora cavernosa. The sections of each ovary were similar and showed normal ovarian structures. There was only one follicle present and that from the right ovary. It was fairly large in size and was lined with normal cells of the stratum granulosum. No germinal follicle was present in this section. Diagnosis: Normal ovarian tissue.

METHODS

Six-hour aliquots of 24 hour urine specimens were analyzed. During collection they were refrigerated, and a small amount of toluol was added as a preservative. The 17-ketosteroid determinations were done by the Zimmerman method as modified by Cahen and Salter. Estrogens were determined colorimetrically by the Kober reaction as developed by Oesterling and Salter and by Salter, Humm and Oesterling. This color reaction is not affected by any stilbestrol present in the sample tested.

HORMONAL EXCRETION STUDIES

Table 1 contains data on Pauline A.'s hormonal excretion levels per 24 hours over a period of 8 months. Except during January 1948, the patient received stilbestrol, 10 mg., daily. During January 1948, she was on 0.05 mg. of estinyl estradiol daily. Since this is a naturally-occurring estrogen, any of it excreted in the urine would be tested by the chemical method used for determination of estrogens or their derivatives in the urine. As can be seen by the tabulation, the levels obtained during this time are higher than the other values obtained during the administration of stilbestrol. The ketosteroid varied a great deal without showing a consistent change. However, it was generally lower by about one-half, except for one value in November, which was equal to the pretreatment level. The FSH determinations, both pretreatment and one obtained 5 months after beginning treatment, are normal. After she had been on 10 mg. of stilbestrol daily for 3 months her breasts had definitely enlarged so that they had an appearance similar to that seen in early puberty. Since that time there has been no further enlargement. There has been no change in her hair distribution or in the rate of growth of her facial hair. She had never had any cramps at regular intervals such as her sister and also had had no spotting. She first noted a slight spotting accompanied by lower abdominal cramps after she had been on medication for 4 months. Since then she has had slight spotting approximately once a month usually accompanied by slight cramps. There have been no marked skin changes. There was no difference noted in her clinical status during the month she was on estradiol as outlined above.

TABLE 1. *Pauline A. Hormone excretion levels per 24 hours*

DATE	17-KETOSTEROIDS	ESTROGEN		FSH	E/A
		Chemical	Bio-assay		
	mg.				
*8/ 1/47	55.8			13	
10/22/47	22.8	4 gamma			0.2
11/29/47	59.0				
1/10/48	11.7	28	6 mouse U	9	2.3
1/24/48	15.5	36	2		2.3
1/29/48	27.3	30			1.1
3/13/48	29.3	18			0.6

* Pretreatment level.

Figure 1 shows Esther's estrogen and androgen urinary excretion levels per 24 hours. All columns up to those marked with specific dates beginning March 8, 1948, are averages of 5 determinations made at intervals of 24 hours. The first column shows the average preoperative level. Postoperatively she was started on 10 mg. of stilbestrol daily which was continued up to February 1948 (12 months). At this point she was given progynon, 6000 U, daily for 2 weeks; then progesterone, 10 mg., for 5 days; then nothing for 1 week. After withdrawal of the hormone therapy there was no bleeding. She was then given 25 mg. stilbestrol for 2 weeks and then stilbestrol, 50 mg., daily for 2 weeks. In the last 2 columns is shown the average excretion levels of 20 normal young adult males and the excretion level of a normal adult female at ovulation. The 17-ketosteroids are plotted in milligrams and the estrogens in micrograms per 24 hours. The values at the bottom of the chart beneath the graph represent the estrogen-androgen ratio for the various determinations. This is an arbitrary value obtained by dividing the estrogen level in micrograms by the androgen level in milligrams per 24 hours. Humm and Salter have shown that normal young adult males have a ratio of one or less, and normal young adult females have a ratio of 7 or more at ovulation.

As can be seen by the chart, E. B.'s average preoperative androgen excretion level was more than 3 times the average value for normal young adult males. Her estrogen level was within the normal range of a non-ovulating female. During the past 14 months, while she has been on stilbestrol, the androgen excretion level has showed wide variations. FSH determinations 3 months and 7 months postoperatively were not elevated. The estrogen excretion level has also showed wide variations, and no correlation has been evident between the androgen and estrogen excretion levels. However, it is evident that the general androgen excretion level is definitely lower than the preoperative level, and that the E/A ratio has consistently remained male in character. At only one time, six months after she had started on stilbestrol, did she even approach a more or less female value (.9). There was no effect during the period of progynon-progesterone administration, February–March, 1948. During the past month she has been receiving a high daily dosage of stilbestrol,—25 mg. for 2 weeks, 50 mg. for three weeks. There has been no further lowering of the androgen excretion level.

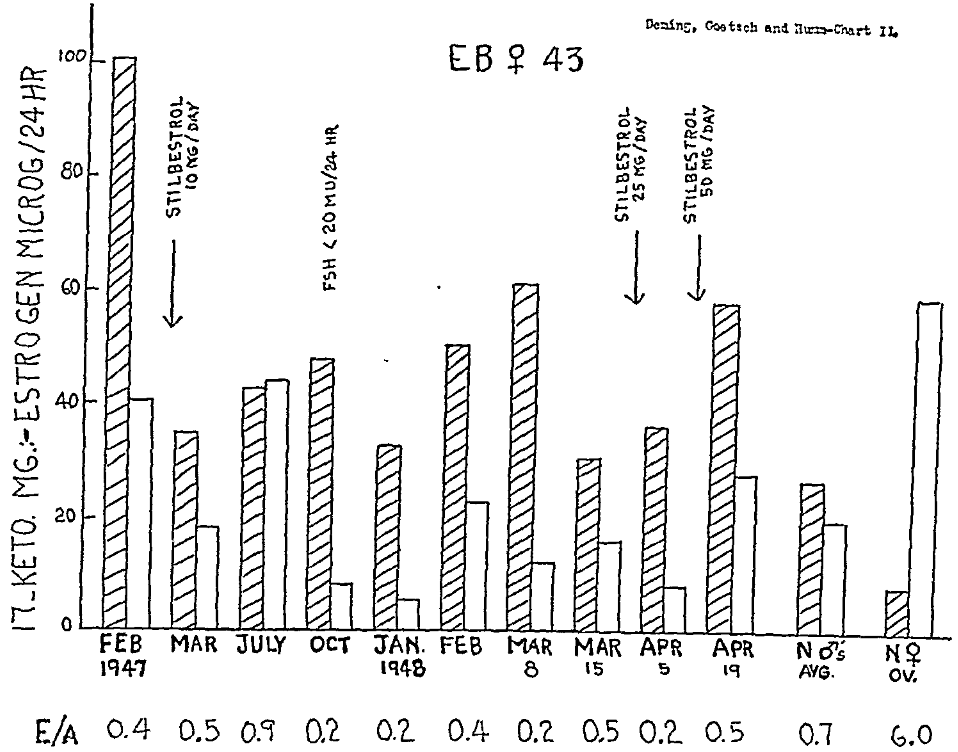


FIG. 1

The clinical course of the patient during this period of study roughly reflects the chemical picture just outlined. Her habitus is still more male than female. However, there have been certain definite changes toward the female side:

1) *Breast changes.* On February 22, 1947, she was started on a daily dose of

10 mg. of stilbestrol. Early in March, she noted tenderness of her breasts and beginning enlargement. The growth of her breasts gradually continued for 6 months and then stopped. The nipples became tender, lost their masculine character and became everted. They have remained essentially stationary since then, if anything, possibly regressing a little. They have the appearance of those of a girl in early puberty.

2) *Hair.* There has been a decrease in the rate of growth of her hair. The hair on the chest has disappeared and that on the abdomen has become sparser. Patches of hair have gone from her legs, and the remainder seems to both her and the observers to be less dense and prominent. The hair of her head seems to be less coarse and is not so heavily streaked with gray. The facial hair decreased in extent over the cheeks but showed no noticeable change in rate of growth until recently, when she was put on a higher dosage of stilbestrol (25 mg. and 50 mg.). Three weeks after starting the higher dose of stilbestrol she reported that the amount of hair shaved from her face each morning was less than it had ever been and that actually she could go longer without shaving.

3) *Vaginal changes.* Prior to the administration of the higher dose of stilbestrol, it was noted that her vaginal mucosa appeared moderately atrophic, as in a senile vaginitis. It was smooth, glistening and dry. The cervix appeared to be very small, and the uterus was also small, both being about one-third normal size. A stain of the vaginal smear revealed slight to moderate cornification of the epithelial cells. After administration of the higher dose of stilbestrol for 3 weeks, the smear showed a much greater estrogenic effect with much more cornification of a larger percentage of the cells. The vaginal mucosa had become grayish-pink, was much more elastic, somewhat wrinkled and moist. The cervix had become much more plainly visible, and seemed to be one-half again as large. The uterus had become more readily palpable and seemed to have increased almost to normal in size.

4) *Menses.* As noted in the present illness, the patient had had cramps regularly each month since the age of 13. She has noted no difference since starting the medication. However, she has had spotting at irregular long intervals associated with the cramps. This is the first time she has ever had any bleeding whatsoever. It has never, however, approached a normal menstrual flow.

5) *Skin.* The skin has become somewhat lighter in color and definitely finer in texture. This is especially notable over the face and chest. She previously had many pimples over the chest, but since the hair in this area has disappeared she has had no further evidence of this.

6) There has been no change in libido. It is interesting to note that this patient also states that at no time did the sensory supply of the clitoris have anything to do with the sensations experienced during coitus. Consequently amputation of the clitoris has had no effect other than to remove an inconvenient appendage.

DISCUSSION

A family with 4 children, 4 of whom were pseudohermaphroditic females, has been presented. To our knowledge this is the largest number of pseudohermaphroditic siblings which has been described. All 4 deformities were con-

This condition is known to be familial. However, since none of the ’s or mother’s relatives are known to have had the condition, and since none he progeny of the fertile siblings have the condition, we have no evidence that is hereditary.

As to the diagnosis made in the cases presented, we feel that although the adrenals have not been biopsied or removed the diagnosis of adrenal virilism is justified. The patients have female reproductive organs. The hormone excretion levels demonstrate marked overactivity of the adrenals. The condition in these patients is congenital, and they have lived to adulthood without evidence of tumor mass or metastatic lesions. At operation in both instances both adrenals were palpated and felt to be normal in size and shape. The exact cellular morphology of the adrenals, however, has not been demonstrated.

Although these patients are sisters and both exhibit congenital adrenal virilism, there are several points of difference as well as similarity. Other than the male hair distribution and hirsutism in which they are similar, Pauline, the younger, is definitely much more feminine than her elder sister, Esther. Her voice is softer and somewhat higher in pitch, and her general behaviour and mannerisms are more female. Her androgen excretion level has not been as high as her sister’s and has not showed as definite a change with medication. Perhaps with continued observation and treatment for as long a period as her sister has already had, more definite changes will become manifest.

It is interesting to note how great a tolerance these patients have for estrogenic drugs. A dose to which a menopausal woman would be completely intolerant has no effect on these patients symptomatically and very little effect physiologically. As was noted recently, a relatively high dose of stilbestrol (10 mg.) as well as a relatively high dose of estradiol (6,000 U/day) did not produce full cornification of the vaginal epithelium in these patients. However, a higher dosage up to 50 mg. of stilbestrol produced cornification. The character of the vaginal secretion is a sensitive indicator of the physiological status of the patient as far as her estrogenic balance is concerned. It is apparent that in the future this indicator of the physiological status of the patient will have to be more closely followed and more closely correlated with the clinical status of the patient and her hormone excretion level than has been done heretofore. It has already been noted that the production of the full estrogenic effect in Esther was accompanied by some clinical improvement. Further observation will be necessary to determine what further effects may become evident.

The fundamental pathological physiology behind the condition of adrenal virilism is still unexplained. Adrenalectomy or partial excision of one or both adrenals has not, as far as the experience recorded in the literature, been successful in restoring these individuals to a normal state. Study of the cellular morphology of the tissue removed has added little if anything to the elucidation of the pathogenesis of the condition. There are some reports of more or less effective hormonal treatment in individual cases. However, they seldom contain data indicating how the pretreatment hormonal pattern of the patient was altered, and they cover only a short period of follow-up. The treatment of

Vol 61 No 2, 1949

Feb 1949

meeting realistic needs
in smooth muscle spasm . . .

The realistic need to allay nervous tension in patients with smooth muscle spasm is met with Syntronal which combines dependable antispasmodic Syntropan with phenobarbital. It selectively inhibits parasympathetic activity, directly relaxes smooth muscle cells and at the same time relieves the causative or accompanying tension. Syntronal is indicated for the relief of spastic disorders of the gastrointestinal and genitourinary tracts, and in dysmenorrhea with uterine muscle spasm. Each sugar-coated tablet contains 50 mg of Syntropan and 15 mg of phenobarbital. Bottles of 30 and 100.

HOFFMANN-LA ROCHE INC. • NUTLEY 10 • N. J.

Syntronal

'Roche'

Syntropan® & Syntronal®

Continued from Front Cover

Cancer of Bladder. *G. J. Thomas.* . 359

Amyloid Tumor of Bladder. *L G. Craig* 365

High Frequency Currents for Transurethral Prostatectomy *H. M Weyrauch, J. B. Bassett and M. M. Berger* 371

Anomalies of Ductus Deferens and Epididymis *L Michelson* 384

Vas Deferens Anastomosis. *B. D Massey and E F Nation* 391

Malignancy in Cryptorchidism *W A. Carroll* 396

Osteitis of Spine *C D. Donahue* 405

Streptomycin in Urogenital Tuberculosis *A. C Abernethy and H. H. Edelbrock* 410

Uterovesical Fistula *C E. Burkland* 418

Periurethral Phlegmons *J. G. Riekert* 424

Discussion 430

Retroperitoneal Cellulitis. *A. F. Turner, L M Orr and J C. Hayward* 432

Vesicocolic Fistula. *F. L Senger* 437

Recto-urethral Fistula; Successful Repair. *L J Kleinsasser, R Smith and O. Griffin* 443

Morphology of Spermatozoa. *O S. Culp and J W Best* 446

Discussion 457

Antibacterial Properties of Mandelamine *J. V. Scudi and C J Duca* 459

A New Anesthetic Lubricant. *A. D Gorfain* 468

A New Disposable Rubber Urinal for Males *C Aberhart* 470

The New York Section will meet on April 20, 1949

Annual Meeting, Southeastern Section, Boca Raton Club, Boca Raton, Florida, March 21, 22, 23, 24, 1949

Annual Meeting, Mid-Atlantic Section, Claridge Hotel, Atlantic City, N. J., March 31, April 1 and 2, 1949

Annual Meeting, South Central Section, Broadmoor Hotel, Colorado Springs, Colo., October 17, 18, 19, 1949

RADON

When interstitial radiation is indicated, the ALL GOLD radon implant is recommended.

Our Radon Implants are ALL GOLD—24 Karat—and excellent for intratumoral implantation.

High temperature sterilization is possible with utmost safety.

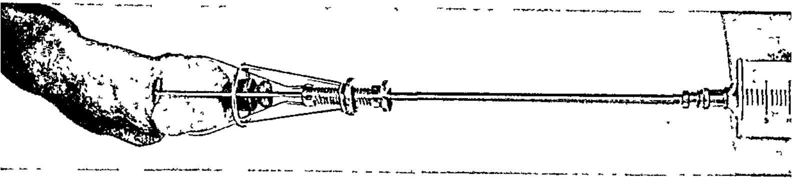
Accurate dosage is assured because the ALL GOLD radon implant is sold with a guarantee as to radon content at hour of use.

Prices and Literature on Request.

RADIUM CHEMICAL COMPANY • Inc.

570 Lexington Ave., New York, 22, N. Y.

Chicago: Marshall Field Annex Building



BRODNY URETHROGRAPHIC CLAMP

Ref: "A New Instrument for Urethrography in the Male" M. Leopold Brodny, M.D., Boston. Journal of Urology, Vol. 46, No. 2, August 1941; "Enuresis—The Use of Cysto-Urethrography in Diagnosis" M. Leopold Brodny, M.D., and Samuel A. Robbins, M.D., Boston, Journal of the A.M.A., December 16, 1944.

The Brodny Urethrographic Clamp was designed to improve the method customarily used in urethrography of the male, namely, manual holding of the glans penis for the introduction of a glass syringe fitted with a rubber acorn tip to obturate the meatus and allow for the injection of the iodized oil into the urethra. The disadvantages of this method are overcome by the use of the Brodny Urethrographic Clamp in that . . .

1. **The operator's hands are not exposed to the x-ray.**
2. **There is no difficulty in obtaining a satisfactory grasp of the glans even when there is leakage of oil.**
3. **It eliminates the strain of holding the syringe in place until the films have been developed and the results checked.**

The Brodny Urethrographic Clamp can also be readily adapted for the injection of measured quantities of medication into the urethra. Here it has the additional advantage of preventing staining of the physician's or the patient's hands.

The Clamp consists of four T-shaped limbs with rubber-covered tips, shaped to conform to the longitudinal contour of the glans. The spring steel limbs can be adjusted to fit any size glans. Through the center of the limb arrangement a cannula with a rubber acorn tip on one end and a syringe on the other end can be pushed distally until the acorn tip enters and completely obturates the meatal opening. The cannula is immobilized by a turn of a lock nut. The cannula is 8¼″ long.

D-950 BRODNY URETHROGRAPHIC CLAMP with rubber acorn tip Each $15.50

D-951 BRODNY URETHROGRAPHIC CLAMP OUTFIT, complete with rubber acorn tip and 30 cc. Gold Seal Hypodermic Syringe, with large-to-small Luer adapter. Each $19.50

Order from your surgical dealer

CLAY-ADAMS COMPANY, INC.
141 EAST 25th STREET · NEW YORK 10
Showrooms also at 308 West Washington Street, CHICAGO 6, ILL.

THE JOURNAL OF UROLOGY

Manuscripts submitted for publication and communications concerning editorial matters should be sent to Dr. J. A. Campbell Colston, Brady Urological Institute, Johns Hopkins Hospital, Baltimore 5, U. S. A.

Reprints of articles will be furnished to contributors when ordered in advance. A table showing cost of reprints, with an order slip, is sent with proof.

THE JOURNAL OF UROLOGY is issued monthly. Two volumes are issued each year beginning in January and July.

Correspondence concerning business matters should be addressed to The Williams & Wilkins Company, Publishers of Scientific Books and Periodicals, Mount Royal and Guilford Avenues, Baltimore, U. S. A.

Subscription price: $5.00 per volume. For countries outside the Postal Union (North and South America and Spain), add 50 cents per volume, for delivery.

Claims for copies lost in the mails must be received within 30 days (domestic). Changes of address must be received within two weeks of the date of issue.

New subscriptions and renewals are entered to begin with the first issue of the current volume. Should any issue of the current volume be out of print at the time the subscription order is received, the pro-rata value of such numbers will be credited to the next volume, and the renewal invoice therefore adjusted accordingly.

Subscriptions should be renewed promptly—To avoid a break in your series, subscriptions should be renewed promptly. The publishers cannot guarantee to supply back issues on belated renewals.

Subscriptions, new or renewal, should be sent to the Publishers or to Agents listed below.

AGENTS

For Australia: Angus & Robertson, Limited, 89–95 Castlereagh Street, Sydney.

For the British Empire, except Australia and Canada: Baillière, Tindall & Cox, 8 Henrietta St., Covent Garden, WC. 2, London, England.

For Canada: Wm. Dawson & Sons Ltd., 70 King Street East, Toronto.

PUBLISHED MONTHLY BY

THE WILLIAMS & WILKINS COMPANY

Publishers of Scientific Books and Periodicals

BALTIMORE-2, U. S. A.

PUBLISHERS OF: *Medicine, Journal of Urology, Journal of Pharmacology and Experimental Therapeutics, American Journal of Tropical Medicine, Journal of Immunology, Journal of Industrial Hygiene and Toxicology, Quarterly Review of Biology, Journal of Bacteriology, Chemical Reviews, Soil Science, Social Forces, Journal of Organic Chemistry, Occupational Therapy and Rehabilitation, The American Journal of Clinical Pathology, Journal of Physical Chemistry, Philosophy of Science, Bacteriological Reviews, Gastroenterology, The Journal of Investigative Dermatology, Obstetrical and Gynecological Survey, Plastic and Reconstructive Surgery.*

Bangkok... calling Burlington

From and *for* every land in which modern surgical methods are known and practiced come new clinical reports on the use of Pentothal Sodium for intravenous anesthesia. Now numbering more than 1130, these reports testify to the widespread and continuing interest of the medical profession in Pentothal Sodium. But more than that, they constitute a detailed, accurate and authoritative guide covering every phase of its use. With such a guide available, Pentothal Sodium for intravenous anesthesia can be used *safely*, *conveniently* and *effectively*. Descriptive literature—reviewing indications and contraindications, advantages and disadvantages, precautions and techniques—will be sent promptly upon request. Just drop a line to ABBOTT LABORATORIES, North Chicago, Illinois.

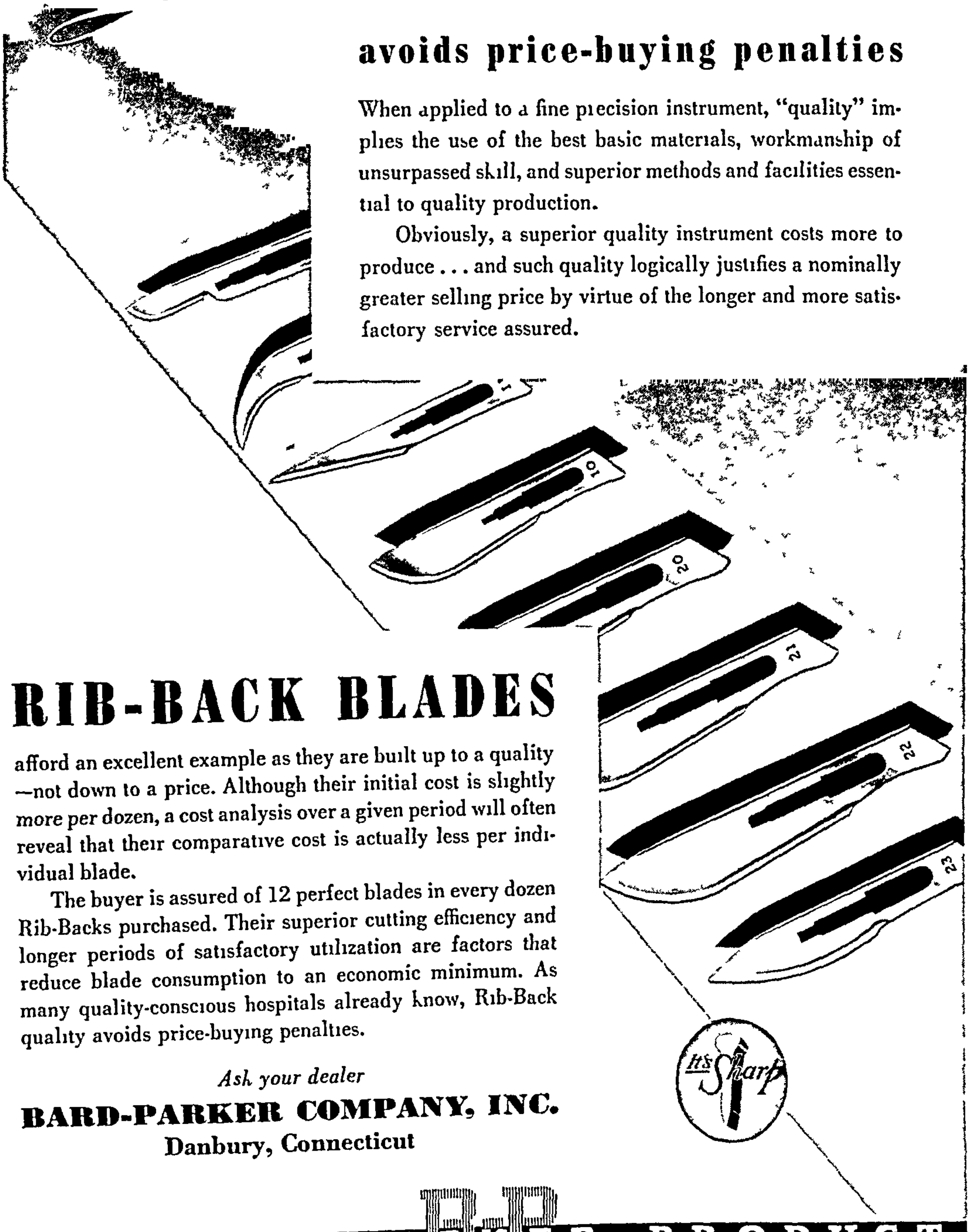
New Pentothal Film

Medical groups interested in a color motion picture showing the uses and limitations of Pentothal Sodium anesthesia in obstetrical procedures may arrange for a showing by writing to Abbott Laboratories, North Chicago, Illinois.

Pentothal® Sodium

(STERILE THIOPENTAL SODIUM, ABBOTT)

FOR INTRAVENOUS ANESTHESIA



Quality

avoids price-buying penalties

When applied to a fine precision instrument, "quality" implies the use of the best basic materials, workmanship of unsurpassed skill, and superior methods and facilities essential to quality production.

Obviously, a superior quality instrument costs more to produce . . . and such quality logically justifies a nominally greater selling price by virtue of the longer and more satisfactory service assured.

RIB-BACK BLADES

afford an excellent example as they are built up to a quality —not down to a price. Although their initial cost is slightly more per dozen, a cost analysis over a given period will often reveal that their comparative cost is actually less per individual blade.

The buyer is assured of 12 perfect blades in every dozen Rib-Backs purchased. Their superior cutting efficiency and longer periods of satisfactory utilization are factors that reduce blade consumption to an economic minimum. As many quality-conscious hospitals already know, Rib-Back quality avoids price-buying penalties.

Ask your dealer

BARD-PARKER COMPANY, INC.

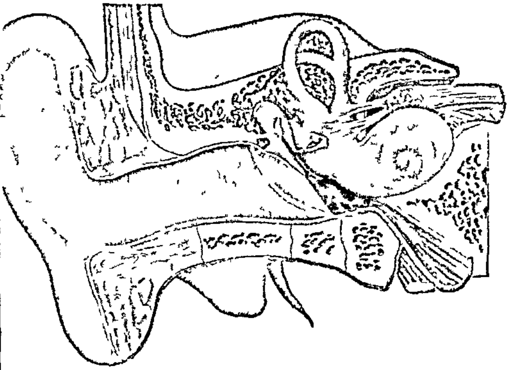
Danbury, Connecticut

A BARD-PARKER PRODUCT

Announcing...

DIHYDROSTREPTOMYCIN

A New, Dramatic Advance In Antibiotic Therapy



- **Extremely Low Incidence of Vestibular Disturbances**

- **Less Frequent Allergic Manifestations**
- **Unsurpassed Purity**
- **Undiminished Antibacterial Activity against *Mycobacterium tuberculosis***

Dihydrostreptomycin Merck is a new, highly purified antibiotic, chemically distinct from streptomycin, and characterized by greatly reduced neurotoxicity.

Allergic manifestations due to dihydrostreptomycin therapy are rare, and no local skin irritation or other allergic phenomena have been reported thus far among personnel who frequently handle this drug.

Dihydrostreptomycin Merck and Streptomycin Calcium Chloride Complex Merck may be used interchangeably in the treatment of tuberculosis.

DIHYDROSTREPTOMYCIN
MERCK
(supplied as the sulfate or the hydrochloride)

MERCK

MERCK & CO., Inc. *Manufacturing Chemists* RAHWAY, N. J.

RETROPUBIC URINARY SURGERY

by Terence Millin, F.R.C.S.

Genito-Urinary Surgeon, London

Gives in detail the methods employed in the retropubic approach to a number of surgical problems

Prostatectomy
Stress Incontinence in Women
Prostatic Obstruction
Fibrous and Calculous Prostate
Carcinoma of the Prostate and Bladder
Pre- and Post-operative Care
Anesthesia

215 pp., 163 figs. $7.00

The Williams & Wilkins Co.

Mt. Royal & Guilford Aves., Baltimore 2, Md.

Those Indefinite Symptoms . . .

Mild states of acidosis resulting in lowered alkali reserve may give rise to such indefinite symptoms as lassitude, fatigue, nausea, sleeplessness and loss of appetite. Relief is often obtained by replenishing the alkali reserve by the administration of Kalak.

Kalak®

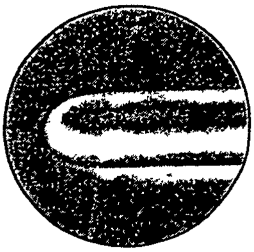
A CARBONATED MULTI-BASE MINERAL WATER

It supplies the chief of the bases of which the reserve is composed. Kalak commends itself because palatable and effective not only at neutralization but in increasing fluid intake. It is excellent adjuvant in all antibiotic therapy.

Available at all pharmacies.

Kalak Water Co. of New York, Inc.
30 Rockefeller Plaza
New York 20, New York

RADON SEEDS

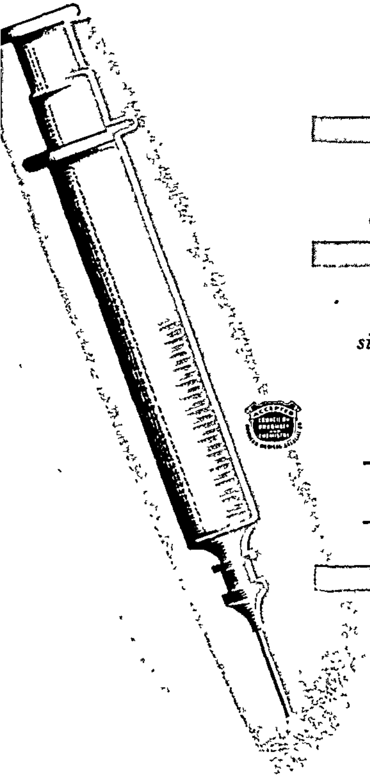


FOR safety and reliability use composite Radon seeds in your cases requiring interstitial radiation. The Composite Radon Seed is the only type of metal Radon Seed having smooth, round, non-cutting ends. In this type of seed, illustrated here highly magnified, Radon is under gas-tight, leak-proof seal. Composite Platinum (or Gold) Radon Seeds and loading-slot instruments for their implantation are available to you exclusively through us. Inquire and order by mail, or preferably by telegraph, reversing charges.

THE RADIUM EMANATION CORPORATION
GRAYBAR BLDG. Telephone MU 3-8636 NEW YORK, N. Y.

(In writing to advertisers, please mention the journal—it helps.)

accurate, safe urography



NEO-IOPAX* IS ACCURATE. Its optimal radiopacity produces clear delineation of the urinary tract permitting diagnostic interpretations to be made confidently.

NEO-IOPAX IS SAFE. Its unblemished record[1]—*more than fifteen years of effective urinary tract visualization without a single fatality reported in the literature*—remains to be equalled. Administered intravenously, using proper technic, NEO-IOPAX is remarkably free from even minor side-effects.[2,3]

NEO-IOPAX

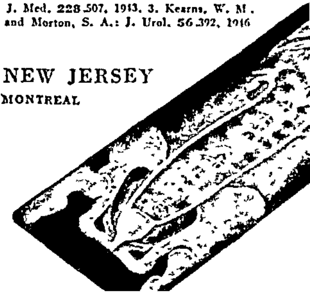
(BRAND OF SODIUM IODOMETHAMATE)

NEO-IOPAX is available as a stable, crystal-clear solution of disodium N-methyl-3, 5-diiodo-chelidamate in 10, 20 and 30 cc. ampuls of 50% concentration and in 10 and 20 cc. ampuls of 75% concentration. Boxes of 1, 5 and 20 ampuls.

BIBLIOGRAPHY: 1. Simon S.: J.A.M.A. 138:127, 1948. 2. Pearman, R. O., New England J. Med. 228:507, 1943. 3. Kearns, W. M., Hefke, H., and Morton, S. A.: J. Urol. 56:392, 1946

*®

CORPORATION • BLOOMFIELD, NEW JERSEY
IN CANADA, SCHERING CORPORATION LIMITED, MONTREAL



New and Valuable Reference Work

Encyclopedia of MEDICAL SOURCES *By* EMERSON CROSBY KELLY, M.D., F.A.C.S. *Associate Professor of Surgery, Albany Medical College. Editor, Medical Classics*

After several experiences in finding errors or incomplete information in references to original work, Dr. Kelly began to keep a list of references to medical eponyms and original investigations. The present compilation is the outgrowth of this list. In it he gives accurately with title and complete reference, the outstanding contributions to medical science, together with medical eponyms such as culture media, methods, signs, syndromes, etc In all, the list includes over 5000 names and 150,000 references. More than ninety percent of the papers have been consulted in the original. The index includes disorders, operations, etc., and provides in effect a completely cross-referenced volume of medical sources. Not only will the book be of great use to medical students and practicing physicians, but librarians and research workers will find it invaluable.

481 pages $7.50

THE WILLIAMS & WILKINS COMPANY
Mt. Royal and Guilford Aves. Baltimore 2, Maryland

WHAT A *Difference!*

THE GOMCO TIDAL IRRIGATOR

Performs complete cycle of irrigation and drainage WITHOUT ATTENTION!

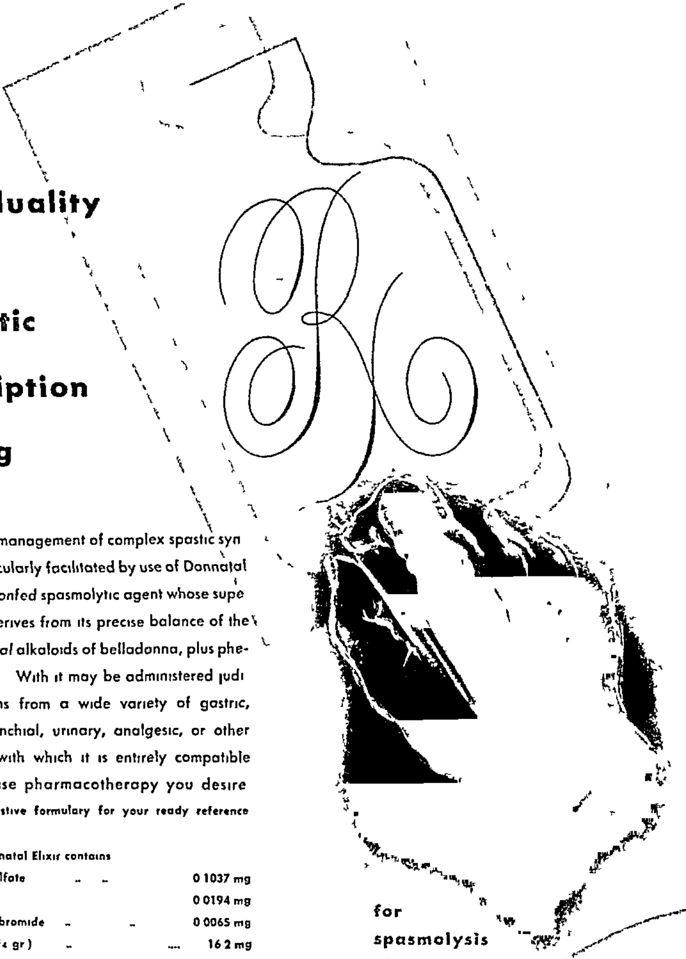
- is easily set up and adjusted to the patient.
- is accurate and dependable.
- is a complete unit, with all parts ready for operation.
- is easy to clean.
- has no moving parts to wear out.
- is in successful use in many hospitals. Uses simple technic.

WRITE FOR NEW DESCRIPTIVE FOLDER on this safe, time-saving, easily operated unit, or see your dealer

A new catalog has just been printed. It is yours for the asking.

GOMCO SURGICAL MANUFACTURING CORP.
836 M. E. Ferry Street Buffalo 11, N. Y.

GOMCO EQUIPMENT
Fostering Improved Technics



individuality in spasmolytic prescription writing

Individualized management of complex spastic syndromes is particularly facilitated by use of Donnatal Elixir—the *spoonfed* spasmolytic agent whose superior efficacy derives from its precise balance of the principal *natural* alkaloids of belladonna, plus phenobarbital • With it may be administered judicious selections from a wide variety of gastric, intestinal, bronchial, urinary, analgesic, or other drug agents with which it is entirely compatible . for the precise pharmacotherapy you desire

Write for suggestive formulary for your ready reference

Each 5cc of Donnatal Elixir contains

Hyoscyamine Sulfate	0 1037 mg
Atropine Sulfate	0 0194 mg
Hyoscine Hydrobromide	0 0065 mg
Phenobarbital (¼ gr)	16 2 mg

Also available as Donnatal Tablets and Donnatal Capsules

for spasmolysis plus

donnatal® elixir Robins

Also available as
Donnatal Tablets
and Donnatal Capsules

A. H. Robins Co , inc.
Ethical Pharmaceuticals of Merit since 1878
Richmond 20, Va.

pain!...

the synergic formula for maximum non-narcotic analgesia

To obtund pain without recourse to narcotics—yet better than the patient's medicine cabinet can—becomes a daily professional obligation. That's why Phenaphen was formulated with calculated pharmacologic precision . . . the analgesic action of its aspirin — phenacetin components being implemented and prolonged by its phenobarbital content (which helps allay apprehension . . . its hyoscyamine further increasing overall efficiency through local anodyne action. Phenaphen —the astute professional prescription for pain — is promoted to physicians only.

Each tablet or capsule contains:

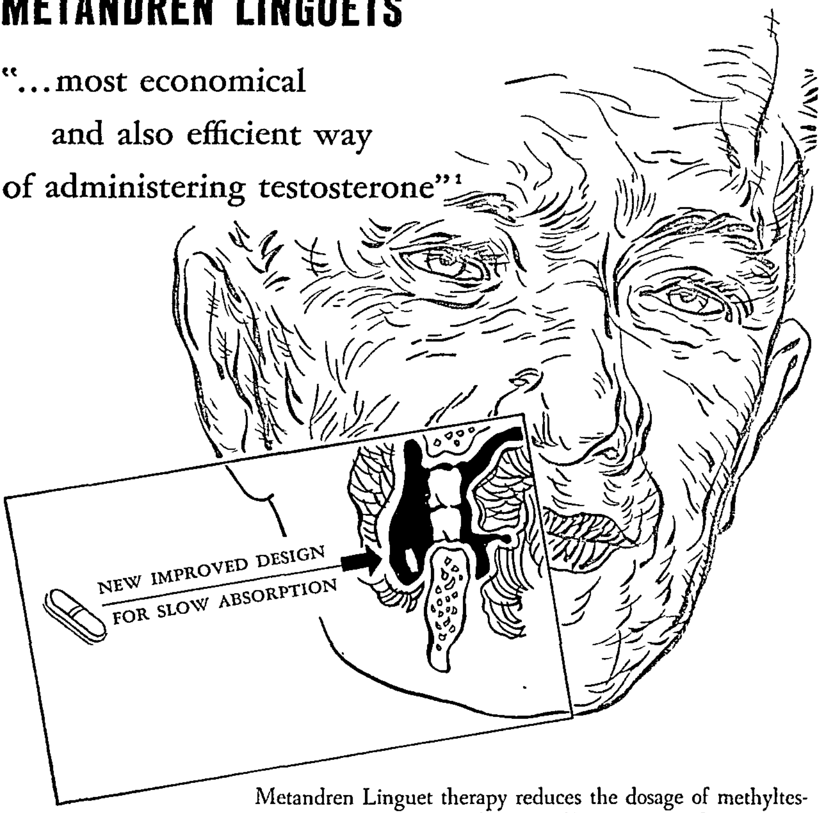
Phenacetin (3 gr.)	**194 mg.**
Acetylsalicylic Acid (2½ gr.)	**162 mg.**
Hyoscyamine Sulfate	**0.03 mg.**
Phenobarbital (¼ gr.)	**16.2 mg.**

● *phenaphen*

A. H. Robins Co., inc.
ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878
Richmond 20, Va.

METANDREN LINGUETS

"...most economical
and also efficient way
of administering testosterone"[1]



Metandren Linguet therapy reduces the dosage of methyltestosterone to approximately one-half that required when this male sex hormone is ingested in tablet form.

The Linguet is specially designed to dissolve *slowly* in the space between gum and cheek or under the tongue. Thus Metandren Linguets are absorbed directly into the systemic circulation, largely avoiding inactivation in the gastrointestinal tract and the liver.

- *Extensive literature on request.*

[1] Lisser, H.: Calif. & West. Med., 64: 177, 1946.

METANDREN LINGUETS — 5 mg. (white) scored; 10 mg. (yellow) scored — in bottles of 30, 100 and 500.

Ciba PHARMACEUTICAL PRODUCTS, INC., SUMMIT, NEW JERSEY

METANDREN, LINGUETS—Trade Marks Reg. U.S. Pat. Off. 2/1136M

NEW ★ BIG ★ IMPORTANT

Textbook of GENITO-URINARY SURGERY

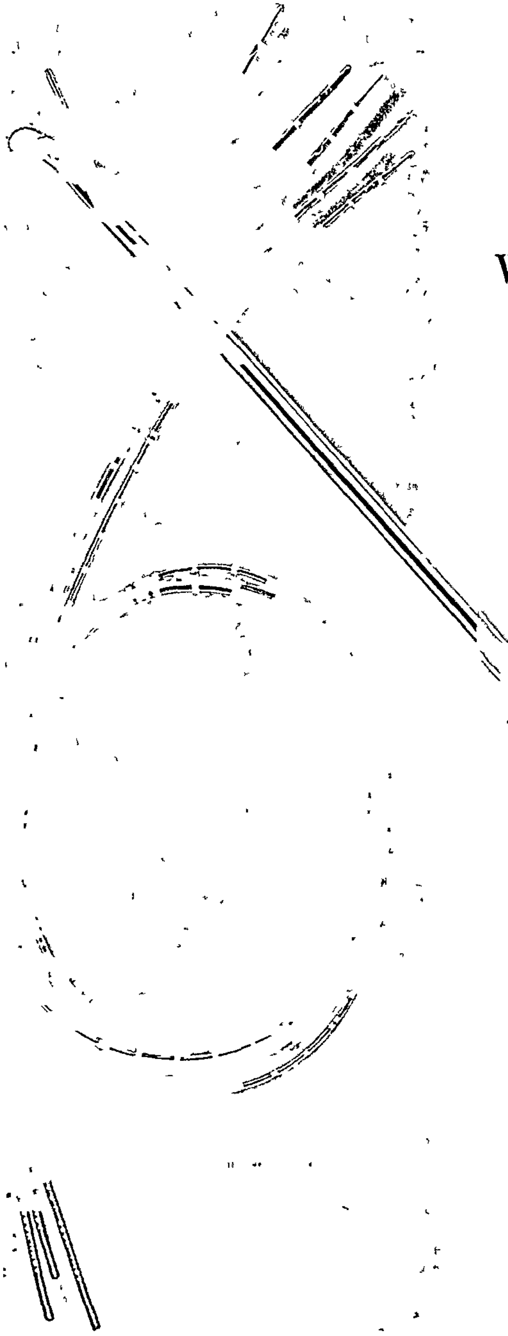
Edited by

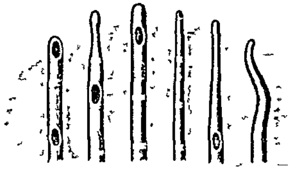
H. P. WINSBURY-WHITE,
M.B., CH.B., F.R.C.S.
Surgeon, St. Paul's Hospital for Genito-Urinary Diseases; Urologist, Princess Elizabeth Hospital for Children; Lecturer in Urology, University of London

Forty of Great Britain's leading surgeons and urologists have contributed to this up to date text covering the urinary tract and the male genital system. Controversial subjects such as the different methods of removing prostatic obstruction are fully discussed. The eighty-three chapters with over four hundred and fifty illustrations cover genito-urinary surgery in all its aspects. Well illustrated, with many figures in color.

1046 pp., 451 figs., $20.00

THE WILLIAMS & WILKINS CO.
Mt. Royal and Guilford Aves. Baltimore 2, Maryland





ACMI
Woven Ureteral Catheters

Serve Better
because they're
Made Better

QUALITY OF CONSTRUCTION is never more essential for flawless performance than in ureteral catheters. Meticulous urologists prefer ACMI woven catheters because of their . . .

Physical Perfection: They're nylon *woven to prevent moisture absorption that* [illegible] Boiling or autoclaving will not destroy their [illegible] ıque material [illegible] ult is—

[illegible] ACMI Cath- [illegible] onstant, rapid drainage. They have just the right flexibility; and [illegible] permits [illegible] markings [illegible] through [illegible]

ACMI Catheters are precise in size (with size markings clearly printed); and are available in X-ray, non X-ray, graduated and non-graduated styles; and with a variety of tips, including whistle, round, olive, and Garceau tapered tips.

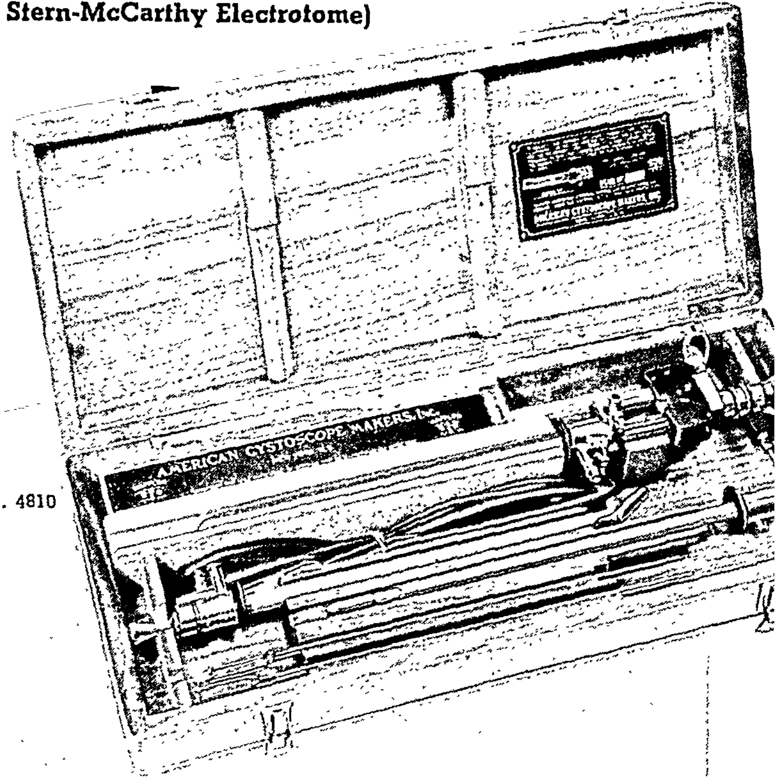
AMERICAN CYSTOSCOPE MAKERS, INC.
1241 LAFAYETTE AVENUE • NEW YORK 59, N Y

First in Cystoscopes — First in Catheters

The Nesbit Convertible Roller Bearing Resectoscope

(Modification of the Stern-McCarthy Electrotome)

A·C·M·I
TRADE MARK



Catalog No. 4810

For wide range utility under a variety of urethra-size requirements . . . and for near-frictionless operation of the working element—this instrument is particularly noteworthy.

The roller bearing construction reduces to an absolute minimum any frictional resistance in the working element . . . which can accommodate either the 24 Fr., 26 Fr., or 28 Fr. sheath, supplied with the instrument.

With the two smaller sheaths, a standard 24 Fr. loop is used; while the largest sheath requires a special 28 Fr. loop with a 24 Fr. stem, two of which are supplied.

The smallest sheath can employ a No. 68 telescope, while the two larger sizes can use either a No. 68 or No. 68A telescope as desired.

Extra 24 Fr. loops, two Timberlake Obturators (24 Fr. and 28 Fr.), and a Stopcock are also provided.

Write for full information

American Cystoscope Makers, Inc.

1241 LAFAYETTE AVE. · FREDERICK J. WALLACE, Pres. · NEW YORK 59, N.Y.

AMERICAN UROLOGICAL ASSOCIATION

OFFICERS 1948–1949

President—Dr. Charles C. Higgins, Cleveland Clinic, Cleveland, Ohio
President-Elect—Dr. Carl F. Rusche, 906 Taft Building, Hollywood, California
Past-President—Dr. Herbert H. Howard, 270 Commonwealth Avenue, Boston, Mass.
Secretary—Dr. Thomas D. Moore, 899 Madison Ave., Memphis, Tenn.
Treasurer—Dr. George C. Prather, 1180 Beacon Street, Brookline, Mass.
Historian—Dr. Wirt B. Dakin, 523 W. Sixth St., Los Angeles, California

EXECUTIVE COMMITTEE

New England Section—Dr. Roger C. Graves, 12 Bay State Rd., Boston, Mass.
Alternate—Dr. Fletcher H. Colby, 262 Beacon St., Boston, Mass.
New York Section—Dr. George W. Fish, 755 Park Avenue, New York, New York
Alternate—Dr. Augustus Harris, 306 Park Place, Brooklyn, New York
Mid-Atlantic Section—Dr. Charles H. deT. Shivers, 121 S. Illinois Ave., Atlantic City, N. J.
Alternate—Dr. Ralph M. LeComte, 1801 Eye St., N.W., Washington, D. C.
Southeastern Section—Dr. Hamilton W. McKay, 121 W. Seventh St., Charlotte, N. C.
Alternate—Dr. J. Ullman Reaves, 303 Van Antwerp Bldg., Mobile, Ala.
North Central Section—Dr. William J. Baker, 7 West Madison Street, Chicago, Illinois
Alternate—Dr. Carroll C. Hyde, 122 N. Lafayette Blvd., South Bend, Ind.
South Central Section—Dr. R. Lee Hoffmann, 1019 Professional Bldg., Kansas City, Mo.
Alternate—Dr. H. Fay H. Jones, 808 Donaghey Bldg., Little Rock, Ark.
Western Section—Dr. Dudley P. Fagerstrom, 710 Medico-Dental Bldg., San Jose, Calif.
Alternate—Dr. A. J. Scholl, 1930 Wilshire Blvd., Los Angeles, Calif.

Sections of the American Urological Association

NEW ENGLAND SECTION

President—Dr. Edward L. Peirson, 374 Essex Street, Salem, Mass.
Secretary-Treasurer—Dr. Richard Chute, 330 Dartmouth Street, Boston 16, Mass.
Executive Committee—Chairman, Dr. George C. Prather, 1180 Beacon Street, Brookline 46, Mass.; Dr. John P. Bowler, Hitchcock Clinic, Hanover, N. H.; Dr. Winthrop M. Flagg, 49 South Winooski Ave., Burlington, Vt.; Dr. Ernest K. Landsteiner, 4 George St., Providence, R. I.; Dr. Samuel A. MacDonald, 1414 Drummond St., Montreal, P. Q., Canada; Dr. Donald F. Marshall, 142 High St., Portland, Maine; Dr. C. H. Neuswanger, 89 N. Main St., Waterbury, Conn.; Dr. Bancroft C. Wheeler, 27 Elm St., Worcester, Mass.

NEW YORK SECTION

President—Dr. Francis P. Twinem, 901 Lexington Ave., New York, N. Y.
Vice-President—Dr. Herbert M. Ill, 42 Woodland Ave., Glen Ridge, N. J.
Secretary—Dr. John N. Robinson, 755 Park Ave., New York, N. Y.
Treasurer—Dr. Oscar P. Schoenemann, 848 Carroll St., Brooklyn, N. Y.
Executive Committee—Dr. John K. de Vries, 144 S. Harrison St., East Orange, N. J.; Dr. George W. Fish, 755 Park Ave., New York, N. Y.; Dr. Augustus L. Harris, 306 Park Place, Brooklyn, N. Y.; Dr. Robert S. Hotchkiss, 65 E. 66th St., New York, N. Y.

NORTHEASTERN SECTION

President—Dr. James C. McClelland, 170 St. George St., Toronto, Ontario
President-Elect—Dr. A. L. Parlow, Medical Arts Bldg., Rochester, New York
Past President—Dr. George E. Slotkin, 333 Linwood Ave., Buffalo, New York
Secretary-Treasurer—Dr. Albert M. Crance, 525 S. Main St., Geneva, N. Y.
Executive Committee—Dr. William A. [illegible]
J. Victor Berry, 180 Metcalfe St [illegible]
kins Arcade, Pittsburgh, Pa.; Dr. [illegible]
N. Y.; Dr. S. A. MacDonald, 1414 Drummond St., Montreal, Que.

MID-ATLANTIC SECTION

President—Dr. Theodore R. Fetter, 255 South 17th Street, Philadelphia 3, Pa.
Vice-President—Dr. Albert E. Goldstein, 3505 N. Charles St., Baltimore 18, Md.
Secy.-Treas.—Dr. Horatio N. Dorman, 611-A Stoneleigh Court, Washington 6, D. C.
Executive Committee—Dr. Grattan G. Irwin, 801 Atlas Bldg., Charleston, W. Va.; Dr. Linwood D. Keyser, Medical Arts Bldg., Roanoke, Va.; Dr. Charles A. W. Uhle, 255 South 17th St., Philadelphia 3, Pa.; Dr. Hugh J. Jewett, 1201 N. Calvert St., Baltimore 2, Md.
Executive Committee of A.U.A.—Dr. Charles H. de T. Shivers, 121 S. Illinois Ave., Atlantic City, N. J.
Alternate—Dr. Ralph M. LeComte, 1801 Eye St., N. W., Washington, D. C.

SOUTHEASTERN SECTION

President—Dr. Harold P. McDonald, 804 Healey Bldg., Atlanta, Ga.
President-Elect—Dr. James J. Ravenel, 96 Ashley Ave., Charleston, S. C.
Past President—Dr. Robert B. McIver, 208 Laura St., Jacksonville, Florida
Secretary-Treasurer—Dr. Russell B. Carson, 314 Sweet Bldg., Ft. Lauderdale, Fla.
Executive Committee—Dr. F. Thomas Boudreau, 705 Merchant Nat'l Bank Bldg., Mobile, Ala.; Dr. Willard L. Fitzgerald, 422 Ingraham Bldg., Miami, Florida; Dr. Stephen T. Brown, 205 Medical Arts Bldg., Atlanta, Georgia; Dr. W. R. Miner, 33 E. Seventh St., Covington, Kentucky; Dr. Hugh T. Beacham, 1110 Pere Marquette Bldg., New Orleans, La.; Dr. Frank L. Ramsay, Ramsay Clinic, Laurel, Mississippi; Dr. Sidney Smith, 421 Professional Bldg., Raleigh, North Carolina; Dr. William R. Barron, 1018 Calhoun St., Columbia, South Carolina; Dr. Samuel L. Raines, 188 S. Bellevue, Memphis, Tenn.
Executive Committee of A.U.A.—Dr. Hamilton McKay, Charlotte, N. C.
Alternate—Dr. J. Ullman Reaves, Mobile, Ala.
Editorial Committee of A.U.A.—Dr. Montague L. Boyd, Atlanta, Ga.

NORTH CENTRAL SECTION

President—Dr. James C. Sargent, 324 E. Wisconsin Ave., Milwaukee 2, Wis.
President-Elect—Dr. Russell D. Herrold, 6 North Michigan Ave., Chicago, Ill.
Secretary-Treasurer—Dr. William J. Engel, 2020 E. 93rd Street, Cleveland 6, Ohio
Executive Committee—Dr. Carroll C. Hyde, 122 N. Lafayette Blvd., South Bend, Ind.; Dr. John L. Emmett, Mayo Clinic, Rochester, Minnesota; Dr. Reed M. Nesbit, University Hospital, Ann Arbor, Mich.; Dr. John B. Wear, 1 S. Pinckney St., Madison 3, Wisconsin; Dr. Leo P. Dolan, 1052 Edison Bldg., 420 Madison Ave., Toledo, Ohio; Dr. Edward M. Honke, 618 Davidson Bldg., Sioux City 13, Iowa; Dr. Robert S. Breakey (*ex-officio*), 1211 Bank of Lansing Bldg., Lansing 16, Michigan; Dr. William J. Baker (*ex-officio*), 7 West Madison St., Chicago 2, Illinois.

SOUTH CENTRAL SECTION

President—Dr. W. Joseph McMartin, 611 City National Bank Bldg., Omaha, Nebr.
Vice-President—Dr. E. Halsell Fite, 7th Fl. Commerce National Bank, Muskogee, Okla.
Secretary-Treasurer—Dr. Harry M. Spence, 4105 Live Oak St., Dallas 1, Texas
Executive Committee—Dr. Neil S. Moore, 729 Frisco Bldg., St. Louis, Missouri; Dr. E. E. Angle, 903 Sharp Bldg., Lincoln, Nebraska; Dr. R. H. Akin, 610 N.W. Ninth St., Oklahoma City, Okla.; Dr. John F. Patton, 723 University Club Bldg., St. Louis, Mo.; Dr. D. R. Higbee, 1117 Republic Bldg., Denver Colorado; Dr. H. E. Neptune, 617 United Life Bldg., Salina, Kansas; Dr. C. M. Crigler, 1006 Esperson Bldg., Houston, Texas; Dr. H. King Wade, Wade Bldg., Hot Springs, Arkansas; Dr. V. E. Berchtold, 206 Coronado Bldg., Santa Fe, N. Mexico; Dr. Santiago Blanco, Calle 60 num. 543, Merida, Yucatan, Mex.

WESTERN SECTION

President—Dr. Arno G. Folte, 870 Market St., San Francisco, Calif.
President-Elect—Dr. George M. Fister, 385 24th St., Ogden, Utah
Past President—Dr. Carl F. Rusche, 1680 N. Vine St., Hollywood, Calif.
Secretary-Treasurer—Dr. Adolph A. Kutzmann, 1930 Wilshire Blvd., Los Angeles, Calif.
Executive Committee—Dr. Samuel K. Bacon, 1680 N. Vine St., Hollywood, Calif.; Dr. Frank J. Clancy, 1305 Fourth Ave., Seattle, Wash.; Dr. Lloyd E. Kindall, 400 29th St., Oakland, Calif.; Dr. Thomas R. Montgomery, 919 Taylor St. Bldg., Portland Oreg.; Dr. Robert J. Prentiss, 233 A Street, San Diego, Calif.; Dr. Russell T. Scott, 307 St. John's Way, Lewiston, Idaho.

(Branch Societies listed on Cover 3)

REGISTRY OF GENITO-URINARY PATHOLOGY

The following members of the Registry of Genito-Urinary Pathology are eager to assist you in registering tumors of the genito-urinary organs, in obtaining the advantages of the consultation service, or in obtaining information regarding the Registry publications or loan sets of microscope slides. Please communicate with the Committee member nearest you regarding the registration of tumors. Communications regarding the other functions of the Registry can be made directly to COL. J. E. ASH, Army Institute of Pathology, Washington, D. C.

CALIFORNIA

TRACY O. POWELL, 915 Equitable Bldg., 6253 Hollywood Blvd., Los Angeles 28
THOMAS E. GIBSON, 450 Sutter St., San Francisco

DISTRICT OF COLUMBIA

COL. J. E. ASH, Army Institute of Pathology, Washington
WILLIAM P. HERBST, 1801 Eye St., N.W., Suite 314, Washington 6

FLORIDA

LOUIS M. ORR, 307 S. Orange Ave., Orlando

GEORGIA

HAROLD P. MCDONALD, The Ballenger-McDonald Clinic, 804–810 Healey Bldg., 57 Forsyth St., Northwest, Atlanta 3

ILLINOIS

WILLIAM J. BAKER, 7 W. Madison St., Chicago 2

INDIANA

WILLIAM NILES WISHARD, JR., 1711 N. Capitol Ave., Indianapolis

IOWA

RUBIN FLOCKS, University Hospitals, Iowa City

LOUISIANA

EDGAR BURNS, Ochsner Clinic, Prytania and Aline Sts., New Orleans 15

MARYLAND

W. HOUSTON TOULSON, Medical Arts Bldg., Baltimore 1

MASSACHUSETTS

RICHARD CHUTE, 330 Dartmouth St., Boston
ROGER C. GRAVES, 12 Bay State Road, Boston
GEORGE C. PRATHER, 1180 Beacon St., Brookline 46

MICHIGAN

REED M. NESBIT, University Hospital, Ann Arbor

MINNESOTA

GERSHOM, J. THOMPSON, Mayo Clinic, Rochester

MISSOURI

NELSE F. OCKERBLAD, 1530 Professional Bldg., Kansas City
E. HUMBER BURFORD, 958 Arcade Bldg., St. Louis
OTTO J. WILHELMI, 218–220 University Club Bldg., St. Louis 3

NEBRASKA

WILLIAM JOSEPH MCMARTIN, 611 City National Bank Bldg., Omaha 2

NEW JERSEY

W. KENNETH WHEELER, 140 Roseville Ave., Newark 7

NEW YORK

Archie L. Dean, 30 E. 40 St., New York City 16
John Newbold Robinson, 180 Fort Washington Ave., New York City 32
E. King Morgan, 52 Remsen St., Brooklyn 2
William A. Milner, 75 Willett St., Albany
Hans R. Sauer, Roswell Park Memorial Institute, 663 N. Oak St., Buffalo 3
W. W. Scott, Medical Arts Bldg., Rochester
Judson B. Gilbert, 1414 Union St., Schenectady 8

NORTH CAROLINA

John E. Dees, Duke University, Durham

OHIO

C. C. Higgins, Cleveland Clinic, Euclid Ave. at 93 St., Cleveland 6

OKLAHOMA

Anson L. Clark, 514 Medical Arts Bldg., Oklahoma City

PENNSYLVANIA

Edward W. Campbell, 1318 Medical Arts Bldg., 16th and Walnut Sts., Philadelphia

TENNESSEE

Samuel L. Raines, 188 S. Bellevue, Memphis 4

TEXAS

R. E. Van Duzen, 721 Medical Arts Bldg., Dallas 1

VIRGINIA

Samuel A. Vest, University of Virginia Hospital, University Station, Charlottesville

WASHINGTON

Alexander B. Hepler, 752 Stimson Bldg., Seattle 1

WISCONSIN

Walter M. Kearns, 238 W. Wisconsin Ave., Milwaukee

CANADA

ONTARIO

Carl Aberhart, 1012 Medical Arts Bldg., Toronto 5

QUEBEC

Magnus I. Seng, Suite 615, 1538 Sherbrooke St., West, Montreal

INSTRUMENT COLLECTION COMMITTEE

The Instrument Collection is made up of urologic instruments and devices given or lent to the American Urological Association. The Collection is to be kept permanently in the Army Medical Museum.

All gifts or loans to the Collection may be sent C.O.D. to Dr. William P. Herbst, 1801 Eye St., N. W., Washington 6, D. C.

J. A. Campbell Colston
William P. Herbst
Thomas J. Kirwin
A. J. Scholl
Montague L. Boyd, Chairman

NOMENCLATURE COMMITTEE

The Nomenclature Committee requests suggestions concerning additions to the published Urological Nomenclature, and also suggestions concerning changes in the present list of accepted diagnoses.

Clyde L. Deming
William J. Engel
John R. Hand
Hugh J. Jewett
Montague L. Boyd, Chairman

The Journal of Urology
Vol. 61, No. 2, February 1949
Printed in U.S.A.

RESECTION OF THE TWELFTH RIB IN THE SURGICAL APPROACH TO THE RENAL FOSSA

FRANK A. HUGHES
From the Department of Urology of the Faculty of Medicine, Montevideo, Uruguay

Surgical exposure of the kidney as practiced in the United States is usually performed by the so-called "standard" or classical lumbar incision. Papin calls this approach the long lumbar incision. It commences in the costomuscular angle, ending near the anterior-superior iliac spine, and is characterized by extensive section of the underlying abdominal muscles. It has the disadvantages of 1) marked surgical trauma to the muscles, 2) incomplete visualization of the superior aspect of the renal fossa and adrenal area, and 3) sequelae of incisional herniae and painful scars. For improved exposure, the lumbocostal ligament is sectioned or preferably the twelth rib is resected. In our country, Surraco has popularized a so-called conservative incision by which the kidney can be exposed for most lesions without trauma to the muscles. He separates the anterior edge of the latissimus dorsi muscle posteriorly and retracts the posterior edge of the external oblique forwards from the costal insertion to the iliac bone. The posterosuperior edge of the internal oblique is pushed downwards and the aponeurosis of the transversus abdominis is incised below the twelfth intercostal and abdominogenital (genitofemoral) nerves.

Ercole in Argentina favors this exposure, calls it the Ekehorn incision, which corresponds to the one Papin describes as the short oblique lumbar incision.

Formerly, we used the classical long lumbar incision and resected the twelfth rib when necessary for better exposure. Ventral hernia followed on occasion. Also it did not seem logical to wait for a surgical difficulty to arise before extending the incision to obtain better exposure. Observation of Surraco's technique led us to the conviction that primary resection of the twelfth rib with separation rather than incision of the muscles was a method of choice. After some experience with this incision we found that upper polar lesions and kidneys with marked perinephritis were exposed with less difficulty than with the usual technique. Therefore it seemed rational to use the newer incision in all kidney operations except when the kidney was obviously low and mobile or where drainage was instituted for pyonephrosis.

Resection of the twelfth rib in kidney surgery has been described and used by various authors. Lichtenberg and Pflaumer in Germany and Heitz-Boyer in France originally resected the rib with incision of the muscles and only later performed the incision as described by Ercole and Surraco. Heitz-Boyer states that there is a strong muscular aponeurotic attachment to the free tip of the twelfth rib which constitutes a rigid, fixed point which often prevents access to the lumbar area. Resection of the rib frees the posterior fibers of the external oblique and the superior fibers of the internal oblique which are inserted into it. This permits relaxation of the lumbocostal ligament and easier mobilization of the muscles. The diaphragm is also inserted by means of the ligamentum arcuatum to the same rib. After removing the rib, the diaphragm and pleura are easily pushed upwards and forwards.

The relationship of the pleural cul de sac to the twelfth rib has been studied from a surgical viewpoint by Minet. This author classifies twelfth ribs into a long type (11 to 14 cm.) and a short type (1.5 to 6 cm.). The long rib is more frequently seen than the short rib, in the proportion of 6 to 1. It is oblique and parallel to the eleventh rib. The short type is generally horizontal or slightly oblique. Ribs of less than 3 cm. are very infrequent, as are so-called medium ribs which measure 7 to 9 cm. The pleural sac passes downwards over the inferior edge of the twelfth rib for 1 or 1.5 cm., reaching the superior edge of the first lumbar vertebra. From this point it goes forward and downwards for 3 or 4 cm., crossing the rib almost horizontally. When the rib is short it is completely adjacent to the pleura. If the rib is longer the pleura is covered by the rib for its posterior 6 cm. and also hidden by the vertebral muscle mass. The pleura crosses the last intercostal space at 10 or 11 cm. from the midline, changes its horizontal or slightly descending direction and then ascends. Summarizing, if the rib is less than 6 cm. long, it is in relation with the pleura in its entirety, whereas if it is long, only the posterior 6 cm. is in relation to the pleura.

TECHNIQUE OF APPROACH

The incision is made directly over the twelfth rib (fig. 1, *A*), which has been carefully palpated, as suggested by Hess. It begins about 8 cm. from the midline and extends to about 2 cm. beyond the costal tip. The fibers of the latissimus dorsi (fig. 1, *B*) as well as those of the serratus posterior inferior (minor) are divided. The rib is exposed, freed subperiosteally and resected (fig. 1, *C*), at the external edge of the vertebral muscles, at which point it is no longer in relation with the pleura. The incision is now prolonged downwards parallel to the direction of the posterior bundles of the external oblique which is freed and pushed forwards. At this point the superior and posterior edges of the internal oblique must be freed and pushed forwards and downwards. When this muscle is too well developed, preventing access to the underlying transversus abdominis its superior fibers may be sectioned. The twelfth intercostal nerve runs under and through the internal oblique in vertical fashion, much more obliquely than the rib, and a few centimetres distant from it. It should be exposed and freed. The aponeurosis of the transversus muscle is next exposed and sectioned on a line parallel to the above mentioned nerve. This incision is made about 1 cm. away from the nerve so that it will not be sutured at the time of closure. After incising the aponeurosis, the pararenal space is exposed. In order to increase the exposure superiorly, the middle and index fingers are introduced into the opening and pushed upwards and backwards (fig. 1, *D*) pushing against the upper fibers of the transversus, the ligamentous tissue and the fibers of the diaphragm which cross and unite with the periosteum of the resected rib. In this way the diaphragm and pleura are separated and ample working space is obtained (fig. 2, *A*). A variation in the procedure after resection of the rib is to incise the lumbodorsal fascia anteriorly, beneath the costal bed (fig. 2, *B*). When the rib is long, this point is protected from the pleura by the diaphragm. The transversus

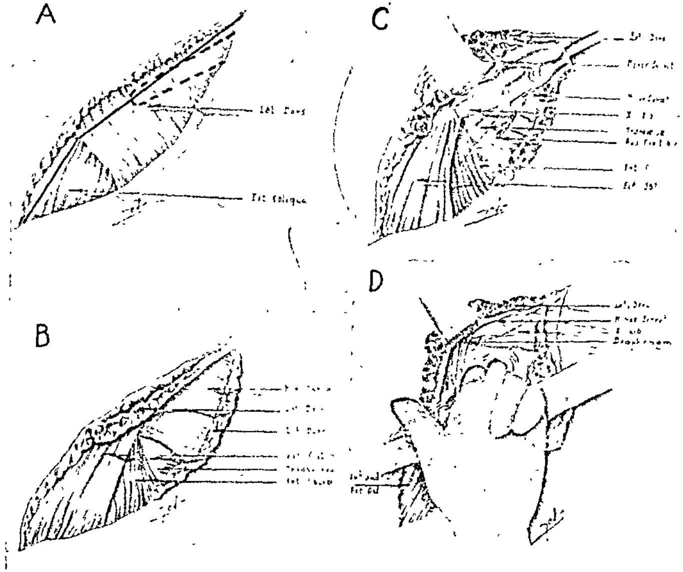

A
C
B
D
Ext Oblique
Diaphragm

FIG 1

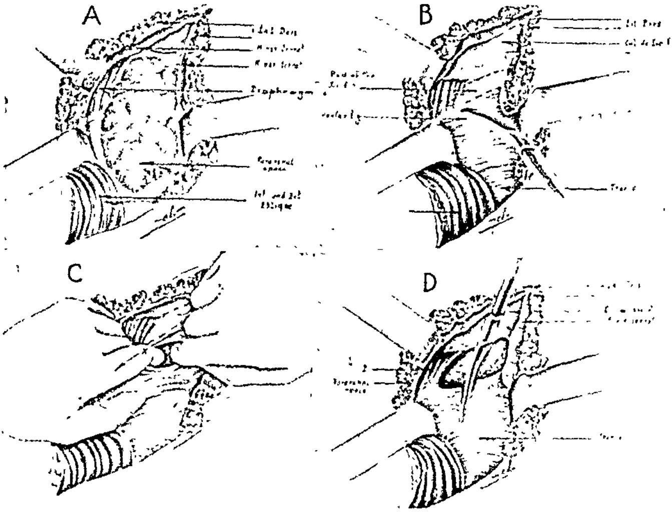

A
B
C
D
Diaphragm
Int and Ext Oblique

FIG. 2

is incised here, separated from the diaphragm (fig. 2, *C*) and sectioned downwards (fig. 2, *D*). Having opened up the lumbar area, incision of Gerota's fascia will permit contact with the kidney.

This author as well as others resects the eleventh rib when the twelfth is short, instead of the twelfth rib.

At the termination of the operation the wound is closed by suturing the transversus muscle and continuing upwards to the diaphragm using interrupted sutures. Care is taken not to include the twelfth intercostal rami nor to pass the needle through the pleural sac. The posterior edge of the external oblique is then approximated to the anterior edge of the latissimus dorsi, which was the only important muscle sectioned. The conservation of the external and internal oblique muscles prevents postoperative hernia.

COMMENT

This surgical approach to the kidney has simplified operative manipulation of the kidney. Hess states: "The ease with which adequate renal exposure can be accomplished by this procedure has been missed by many urological surgeons. The advantages of this approach to the kidney so far offset its possible disadvantages, that it seems rather remarkable that so few American urologists have adopted the procedure." The exposure has been ample and comfortable and prevented excessive bending and the need of brutal retraction. In spite of limited division of muscles, the superior pole of the kidney and renal pedicle are easily accessible.

In discussing Hess' work, Colston made some important remarks. He stressed the value of this incision and the lack of interest shown in it by the American literature. Fear of opening the pleura has been, perhaps, the bugbear which has prevented its wider adoption. However, with modern positive pressure anesthesia, this should afford no threat to the operator. Colston believes that rib resection should be performed in all cases in which an adequate exposure is needed, as determined by the preoperative diagnosis of the position of the kidney or tumor. The indications for this incision are as follows: 1) Exposure of the upper portion of the kidney; 2) plastic operations on the renal pelvis; 3) removal of a large part of the perirenal tissue (tuberculosis); 4) exposure of the renal pedicle with the least manipulation of the kidney (tumors of the kidney); and 5) exposure of the adrenal glands.

SUMMARY

The method of exposure of the renal fossa with initial twelfth rib resection has been described and its advantages enumerated.

REFERENCES

Ercole, R.: An. de cir., **3:** 195, 1937.

Hess, E.: J. Urol., **42:** 943, 1939.

Minet, J.: Arch. d. mal. d. Reins., **9:** 47, 1935.

Papin, E.: Chirurgie du Rein. Paris: Gaston Doin, 1928.

Pflaumer, E.: München med. Wchnschr., **76:** 1640, 1929.

Surraco, L.: Anales del Departmento Científico de Salud Pública, **1:** 144, 1933.

——: El Drenaje Infraperitoneal. Montevideo: Imprenta Rosgal, 1938.

THE JOURNAL OF UROLOGY
Vol. 61, No 2, February 1949
Printed in U.S.A.

MANAGEMENT OF ACUTE NONOBSTRUCTIVE RENAL INSUFFICIENCY[1]

H. EVANS LEITER, IRVING G. KROOP[2], A. FISHMAN AND ABRAHAM HYMAN
From the Mount Sinai Hospital, New York, N. Y.

It is beyond the scope of this presentation to consider all the manifold ramifications involved in the problem of acute renal insufficiency. The kidneys are a major mechanism for the regulation of various equilibria within the body. These include the control of water, electrolytes, nonelectrolytes, hydrogen ion concentration and osmotic pressure. Glomerular filtration and selective activity by the tubules influence the composition of the interstitial and intracellular fluids. The kidneys receive approximately 20 per cent of the total minute output of the heart although they represent about 0.5 per cent of the average body weight. Cessation of renal function would therefore cause drastic alterations in the various equilibria. When one considers the serious effects resulting from the disturbance of a single ion (sodium in Addison's disease, potassium in infantile diarrhoea, chloride in pyloric obstruction), it becomes evident that the artificial control of the many chemical equilibria in renal insufficiency is not easy.

Nevertheless, because of the work by Peters, Smith, Van Slyke, Gamble, and many other investigators, we are in a better position today to cope intelligently with some of the problems resulting from the loss of renal activity. The prognosis in acute renal insufficiency is largely dependent upon two basic conditions. First, the reversibility of the renal lesion with the capacity of the kidney to recover adequate function. Second, our ability to maintain artificially within physiologic limits the various equilibria of the extracellular fluid until such recovery takes place. Such an attitude was taken in a series of cases of anuria and severe oliguria which came under our care during the past year.[3] We were struck by the fact that some of the patients who were referred for treatment, entered the hospital either overloaded with fluids and salt or in a state of severe acidosis or alkalosis. Properly directed and planned therapy begins with the onset of anuria or oliguria and continues until recovery has taken place.

Table 1 classifies the causes of acute renal insufficiency. These are types of cases in which recovery of renal function is possible. In a series of cases of intravascular hemolysis collected by Burwell, 80 per cent of those who died succumbed by the tenth day, while in the group that recovered, 75 per cent developed diuresis between the seventh and eleventh days. Although not always evident, the etiologic cause of acute renal insufficiency plays an important role in both prognosis and treatment.

Table 2 classifies our series of cases from the standpoints of etiology, highest level of the blood urea nitrogen, lowest blood CO_2 content, day of onset of diuresis, type of treatment and the result. It must be emphasized that some of these patients entered the hospital in very poor condition. Case 10 was admitted in pulmonary edema due to the administration of 10,000 cc fluid during the preceding 36 hours in an effort to overcome anuria. Case 11 entered with severe heart failure and acidosis; we were permitted to use the artificial kidney because the outlook seemed hopeless. Whenever possible, the patients were first treated medically in an effort to control the water, electrolyte and acid-base balances. Other measures were utilized when indicated. The artificial kidney was new to us and its use was advised with caution. Although some of these cases are being reported separately in greater detail, we wish to present at this time the clinical course in a few illustrative instances.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 18, 1948.

[2] Dazian Foundation Research Fellow in Medicine.

[3] This series of cases does not represent all instances of acute renal insufficiency admitted to the hospital but only the cases studied by this group.

TABLE I. *Cases of acute uremia in which return or improvement of renal function can occur*

- I. Glomerulonephritis
  - 1. Primary, acute, with anuria
  - 2. Chronic, with low grade azotemia aggravated by intercurrent infection or surgical illness
- II. Lower nephron nephrosis (Lucké)
  - 1. Anuria or oliguria following shock
  - 2. Burns
  - 3. Crush syndrome, blast injuries; hemorrhage into uterine muscle
  - 4. Incompatible blood transfusion
  - 5. Anuria or oliguria following acidosis or alkalosis
  - 6. Sulfonamide intoxication (nonobstructive)
  - 7. Heat stroke
  - 8. Hemoglobinuric nephrosis following transurethral resection
- III. Poisonings
  - 1. Arsenic, mercury, and other heavy metals
  - 2. Carbon tetrachloride
  - 3. Alkali
  - 4. Isopropyl alcohol; phenol
  - 5. Mussel; mushroom
- IV. "Reflex" anuria
  - 1. Post-cystoscopy anuria
- V. Hepatorenal syndrome.

Figure 1 shows the fluid intake, urinary output, blood urea nitrogen and carbon dioxide content in a case of oliguira which followed a transurethral prostatectomy. One can see that the urinary output did not reach 1000 cc daily until the fourteenth day after operation. The total net daily fluid intake during this period averaged less than 2000 cc. Acidosis was treated early with sodium lactate.

Figure 2 represents the clinical course in a case of anuria due to the ingestion of 2.5 gm. mercuric chloride. Note that during the first 48 hours the fluids were administered in excess of 2500 cc daily to balance the loss caused by vomiting and diarrhea. Note also that during the subsequent period of oliguria the administration of fluids was limited to about 500 cc per day. Diuresis began on the eighth day. The use of British anti-Lewisite (BAL) may have helped in the recovery.

TABLE 2

	ADM. NO.	ETIOLOGY	HIGHEST BLOOD UREA IN	LOWEST CO_2	ONSET DIURESIS	TREATMENT	RESULTS AND REMARKS
			mg. %	vol. %			
1	566778	Shock; transurethral prostatectomy	180	33.2	14th day	Medical	Recovery
2	565764	Suprapubic prostatectomy; pulmonary embolus; shock	134	29.1	5th day	Medical	Recovery; urine S.G. 3 mos. later 1.022
3	566362	Shock, post-cesarian; incompat. transf. Hgb. 35% on admission	136	32 on 19th day 86 on 4th day	9th day	Medical	Recovery; pt. admitted with marked edema and alkalosis due to overtreatment with water and alkali
4	555585	Bilateral pyelonephritis; rt. ureter calculus	130	62		Ureterotomy, bilateral decapsulation 2nd day	Died 8th day
5	564084	Bichloride of mercury poisoning	130	20	8th day	Medical	Recovery
6	566387	Post-cystoscopy. Anuria and oliguria	185	23.3	13th day	Medical	Recovery
7	564277	Poisoning? Central necrosis, liver	97	38		Medical	Died; entered hospital in pulmonary edema; 10,000 cc. i.v. in 48 hrs. Died 24 hrs. after admis.
8	568663	Cesarian section; incompat. transf.	85	23		Medical	Died 9th day; overloaded with fluids prior to admission
9	571885	Poisoning?	88	53	10th day	Medical	Recovery

TABLE 2—*Continued*

	ADM. NO.	ETIOLOGY	HIGHEST BLOOD UREA IN	LOWEST CO_2	ONSET DIURESIS	TREATMENT	RESULTS AND REMARKS
			gm. %	*vol. %*			
10	575266	Sulfadiazine poisoning	120	20	9th day	Medical	Recovery; entered hospital with bilateral hydrothorax, anasarca, anuria
11	564328	Post-cystoscopy	244	35.1		Artificial kidney 8th day for 4 hrs.	Died 12 hrs. after artificial kidney. Pt. distended, preterminal and in coma at time of artificial kidney
12	567016	Shock; incompat. transf.; abdominoperineal resection.	142	37.0		Artificial kidney 8th day for 8 hrs.	Died 12th day. Entered artificial kidney in semi-coma. Urea N. dropped from 142 to 92 mg.%. Stayed in coma; 11th day urine 725 cc.
13	567632	Post-abortion; potass. permanganate tablets in vagina	Before dialysis 245 After dialysis 195	12.1		Artificial kidney 12th day for 2 hrs.	Died 14th day. Entered in pulmonary edema and severe acidosis
14	572170	Shock; ligature rt. hepatic art.; hepatorenal syndrome	Before dialysis 107 After dialysis 69	39.4		Artificial kidney 6th day anuria for 2 hrs.	Died 10 days after onset. Artificial kidney used 6 days postcholecystectomy. Discontinued because of bleeding from sinus tract
15	575849	Bichloride of mercury poisoning	Before dialysis 110 After dialysis 30	26	12th	Artificial kidney 6th day for 6 hrs.	Recovered. Sharp drop in blood urea N. from 110 to 30 mg.% with artificial kidney
16	579083	Carbon tetrachloride poisoning	109	36.5	19th	Artificial kidney 8th day 6 hrs. 14th day 6 hrs.	Recovery. Course complicated by vomiting and low prothrombin level with tendency to bleed. 1st dialysis 8th day. Pre- 109. Post- 69. 2nd dialysis 14th day. Pre- 98. Post- 57
17	572403	Bleeding peptic ulcer; shock; incompat.	91	39.7		Peritoneal lavage 6th day	Died 9th day. Peritoneal lavage by Drs. Oppenheimer and Rosenak

We had another case (No. 15) of corrosive sublimate poisoning that was admitted on the fourth day of anuria. There was extensive necrosis and sloughing of the vulva which was the site of introduction of 3 gm. of sublimate in an attempt at abortion. On the evening of admission the artificial kidney was applied for a period of 6 hours. Definite clinical improvement was noted during

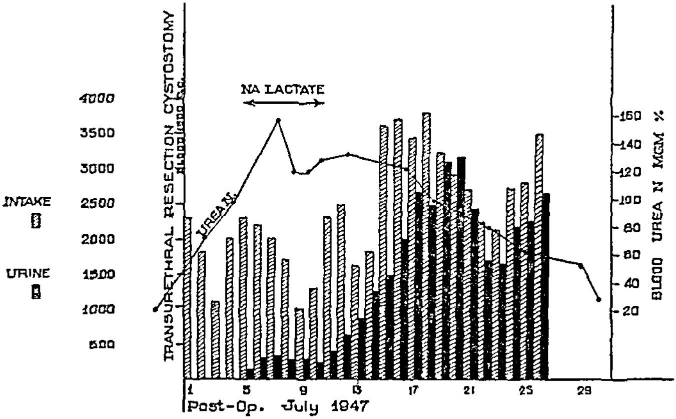


FIG. 1. Case 1. Oliguria following transurethral prostatectomy. Note onset of diuresi on fourteenth day.

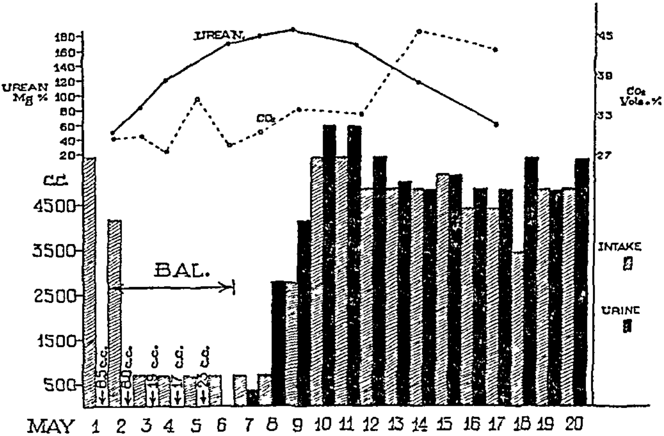


FIG. 2. Case 5. Anuria due to ingestion of 2.5 gm. bichloride of mercury. Note onset of diuresis of eighth day.

the procedure; the blood nitrogen values decreased sharply. This patient recovered.

In figure 3 the patient was admitted after 4 days of anuria due to sulfonamides. Although the drug had been stopped 7 days previously, the blood sulfadiazine level was still 9 mg. per cent. On admission the patient was found to be overloaded with fluids. She had bilateral hydrothorax, moderate anasarca and some fluid in the abdomen. Bilateral thoracentesis was performed. Note the marked restriction of fluids during the first few days and the onset of diuresis on the ninth day. With the development of cardiac failure the urinary output dropped and the blood urea nitrogen rose. Although this patient recovered from the phase of anuria, we believe that she either had previously damaged kidneys or suffered irreparable renal damage.

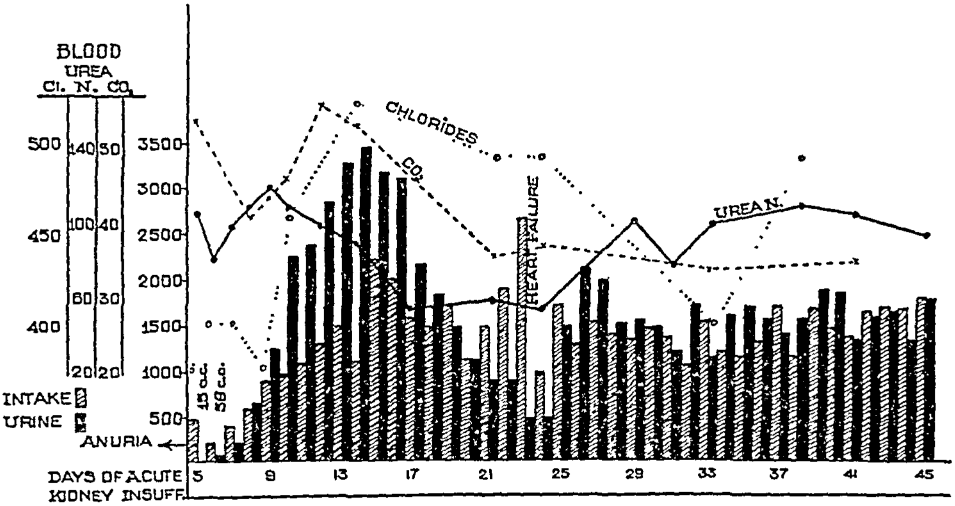


FIG. 3. Case 10. Anuria due to sulfadiazine poisoning. Patient admitted with generalized anasarca. Note onset of diuresis on ninth day. Also note development of oliguria and rise in blood urea nitrogen with onset of heart failure.

DISCUSSION

The treatment of anuria or severe oliguria may be divided into the early, the continued, and the recovery phases of acute renal insufficiency.

Early phase. In some instances, properly directed treatment may shorten or prevent the phase of persistent renal shutdown. The early use of BAL in bichloride of mercury poisoning has improved the prognosis. The appropriate use of antibiotics may control infections which can lead to lower nephrone nephrosis. Clinical shock (according to Mallory) is a major cause of tubular damage. It should therefore be prevented and combated early. Prerenal deviation must be recognized early and treated with parenteral fluids containing the lost electrolytes. Isotonic sodium sulphate solution has been shown to be effective experimentally in dogs with marked hemoglobinemia (Necheles); it may be useful in cases of intravascular hemolysis. The use of alkalies to prevent the precipitation of methemoglobin in the tubules is controversial. Anoxia of the kidney should be avoided. Paravertebral novocaine block has been advocated to counteract renal vasospasm. That vascular spasm occurs has been shown by the experiments of Trueta and in the study of renal blood flow during shock by Cournand and his co-workers.

Phase of persistent oliguria or anuria. During this period, efforts should be made to maintain fluid and electrolyte balance in the extracellular fluid. The fluid intake should balance the fluid loss. Normally, about 1000 cc water is lost through the skin and respiratory tract. The total water intake includes the liquid given by mouth or parenterally, the water contained in the solid food, the water released by the oxidation of carbohydrates, and the preformed water which is freed by the metabolism of tissue fat and protein. Excessive perspiration or gastro-intestinal loss must be supplemented. Since the diet is usually inadequate in calories, overloading with fluids would be represented by a gain in weight. Oral liquids are preferred and excesses can be rejected by vomiting more readily than if given by the parenteral route.

Sodium chloride is given cautiously unless lost by vomiting. Each gram of salt absorbed by the body will hold about 100 cc of water to maintain isotonicity, and unless excreted it will accumulate in the extracellular space. During the phase of anuria it serves no useful purpose unless specifically lost. On the other hand, the administration of sodium lactate or bicarbonate leaves available base for neutralization of organic and inorganic acid radicals. Ampoules of sodium bicarbonate are now available for intravenous use. The large amount of base in a small volume gives it advantages over the use of one-sixth molar sodium lactate solution.

We have been prescribing a diet which consists almost entirely of fruit juices. Since recovery usually occurs within 14 days, the temporary negative nitrogen balance is not of great moment. It has several advantages. Additional base is provided. Carbohydrates have a sparing effect on sodium and on proteins and help in oxidizing some oxy-acids. No external nitrogen is added to a body economy which cannot eliminate the waste products. Lastly, it has been shown in rats that a very low protein diet improves the prognosis of renal insufficiency (Addis, Farr and Smadel).

Elimination of the products of catabolism. It is possible to remove electrolytes and nonelectrolytes by dialysis. However, its use for electrolytes is fraught with danger at the present time. Dialysis is ideal for the elimination of nonprotein nitrogen from the blood. Internal dialysis includes the methods of continuous gastric lavage (Vermooten); irrigation of one isolated loop of small bowel; irrigation and suction through a two-way tube introduced orally into the small bowel (Oppenheimer and Rosenak); and peritoneal lavage (Fine et al.). In these procedures the gastro-intestinal mucosa or peritoneum is used as the dialyzing membrane. Carefully composed solutions must be used or else a rapid loss of electrolytes may result. Internal dialysis usually requires treatment over a period of days. Not all types of cases are suitable for this method, which also has certain inherent dangers.

External dialysis is the procedure wherein the blood is circulated outside the body in a dialyzing system. Such so-called artificial kidneys have been constructed by Kolff, Gordon-Murray and Alwall. Heparin must be used to prevent the blood from clotting; this makes the method hazardous in patients who have a tendency to bleeding. Large amounts of nonprotein nitrogen can be removed in a period of a few hours. In one of our cases the blood urea nitrogen was lowered from 110 mg. per cent to 30 mg. per cent with 6 hours of dialysis. We have been using the Kolff kidney, which is efficient and comparatively safe. Much smaller doses of heparin are now being used than have been advocated.

The major difficulty is to decide when dialysis should be applied. We believe that it is best used when the blood urea nitrogen is high, the patient is in fair condition, and the expected time of renal recovery may be several days away.

Phase of recovery. This is heralded by a progressive increase in the urinary output. During this phase, the various balances may be disturbed by the large loss of electrolytes in the urine as a result of inefficiency of the tubular cells. Unless there has been sodium chloride retention, the addition of salt may be necessary to replace its loss in the urine. Estimation of the urinary chlorides in the total daily urine is of value. Frequent small transfusions are needed to combat the anemia. Human albumin may help some cases (Thorn). Diarrhea is frequent during this period so that excess water and electrolytes may be lost.

Based upon the foregoing discussion, frequent examinations are made and charted. Fluid intake, loss, and body weight are recorded daily. The blood is examined each day for its urea nitrogen, chloride and CO_2 content. Less frequent determinations are made of the blood count, hematocrit, total protein, calcium, phosphorus and potassium in the blood. These measurements are helpful in the artificial regulation of some of the chemical equilibria.

The use of renal decapsulation should also be mentioned. The reports by Abeshouse and Culpepper show a number of favorable results. The procedure is supposedly most useful in the tense, edematous kidney. The effect of increased intrarenal pressure upon renal secretion by Peters would lend support to those advocating decapsulation. Clinical results are difficult to evaluate because the procedure is most often used at a time when spontaneous diuresis may set in. As stated by Thorn, the value of the method would be unquestioned in a case where unilateral decapsulation would be followed by diuresis from the operated but not from the unoperated kidney.

SUMMARY

Recovery from acute renal insufficiency depends upon the ability of the kidney to resume adequate function and upon the success with which we can artificially maintain the physiologic balance of various equilibria.

Some of our experiences in cases of acute renal shutdown have been presented. Dialysis is a valuable adjuvant for the removal of products of catabolism from the extracellular fluid.

45 E. 85th St., New York, N. Y.

REFERENCES

Abeshouse, B. S.: Renal decapsulation: A review of the literature and report of 10 cases. J. Urol., 53: 27, 1945.

Addis, T.: Osmotic work of the kidney and treatment of glomerulonephritis. Tr. A. Am. Physicians, 55: 223, 1940.

Alwall, N.: On the artificial kidney; apparatus of dialysis of the blood in vivo. Acta Medica Scandinavica, 128: 317–325, 1947.

Alwall, N. and Norvitt, L.: On artificial kidney. II. The effectivity of. Acta Medica Scandinavica, supple. 196, pp. 250–258, 1947.

Bradley, S. E.: Medical progress: Biochemical abnormalities during renal insufficiency. New Eng. J. Med., 235: 755 and 791, 1946.

Burwell, E. L., Kinney, T. O. and Finch, C. A.: Renal damage following intravascular hemolysis. New Eng. J. Med., 237: 657, 1947.

Cournand, A., Riley, R. L., Bradley, et al.: Studies of the circulation in clinical shock. Surgery, 13: 964, 1943.

Culpepper, W. S. and Findley, T.: Renal decapsulation for oliguria and anuria. Am. J. Med. Sci., 214: 100, 1947.

Darrow, D. C.: Disturbance in electrolyte metabolism in man and their management. Bull. N. Y. Acad. Med., 24: 147, 1948.

Farr, L. E. and Smadel, J. E.: Effect of dietary protein on course of nephrotoxic nephritis in rats. J. Exp. Med., 70: 615, 1939.

Fine, J., Frank, H. A. and Seligman, A. M.: The treatment of acute renal failure by peritoneal irrigation. Ann. Surg., 124: 857, 1946.

Fishman, A., Kroop, I., Hyman, A. and Leiter, H. E.: Management of anuria in acute mercurial poisoning. New York State J. Med. In press.

Fishman, A., Kroop, I., Leiter, H. E. and Hyman, A.: Experiences with the Kolff artificial kidney. To be published.

Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid. Cambridge, Mass.: Harvard University Press, 1947.

at the Mount Sinai Hospital, New York, N. Y., 1948.
Hampen, Holland: J. H. Kok, N.U., 1946.

H. E. and Hyman, A.: Acute renal insufficiency follow- Treatment. J. Mt. Sinai Hosp. In press.

Lanson, H. D., Bradley, S. E. and Cournand, A.: The renal circulation in shock. J. Clin. Invest., 23: 381, 1944.

Leiter, H. E., Hyman, A., Kroop, I. and Fishman, A.: Acute renal insufficiency following prostatectomy; report of 3 cases. To be published.

Lucké, B.: Lower nephron nephrosis. Mil. Surg., 99: 371, 1946.

Mallory, T. B.: Hemoglobinuria nephrosis in traumatic shock. Am. J. Clin. Invest., 17: 477, 1947.

Newburgh, L. H., Johnst damental principles of metabolism. Ann

Newburgh, L. H.: Renal Bull. N. Y. Acad. Med., 24: 137, 1948.

Olson, W. H. and Necheles, H.: *Studies on anuria. Effect of infusion fluids and diure-* Gynec. & Obst., 84: 283, 1947.

Opp gation in treatment of certain types

Pet in Man. Springfield, Ill.: Charles C. Thomas, 1935.

——: Water Balance in Health and in Disease. See Diseases of Metabolism by G. G. Duncan. Philadelphia: W. B. Saunders Co., pp. 271–346.

Peters, J. T.: Oliguria and anuria due to increased intrarenal pressure. Ann. Int. Med., 23: 221, 1945.

Sellers, E. A. and Gornall, A. G.: *Intestinal perfusion in treatment of uremia.* Science, 106: 108, 1947.

Smith, H. W.: The Physiology of the Kidney. New York: Oxford University Press, 1937.

Thorn, G. W., Koepf, G. F. and Clinton, M., Jr.: Renal failure simulating adrenocortical insufficiency. New Eng. J. Med., 231: 76, 1944.

Thorn, G. W.: *Treatment of renal insufficiency.* J. Urol., 59: 119, 1948.

Trueta, J., Barclay, A. E., Daniel, P. M. et al.: Studies of the Renal Circulation. Oxford, Eng.: Blackwell Scientific Pub., 1947.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DISCUSSION

DR. GEORGE W. THORN (Boston, Mass.): It is a great pleasure to me to be here again this year, and I think the paper represents a great field for improvement in our present mortality statistics.

I was very much interested in the experiments which Dr. Leiter and Dr. Hyman presented, and I was also very glad that they, too, took the opportunity to point out to you that a good many of these patients can be treated successfully by relatively conservative measures, and indeed I suspect that the majority can be or will be handled by that method.

The artificial kidney, along with peritoneal irrigation and the use of the stomach and small intestine as dialyzing membranes, will be used from time to time in the more severe cases of anuria and azotemia. In the majority of cases, however, I believe conservative methods will suffice.

There are still many aspects of the artificial kidney which one can improve upon, and I suspect that some of the early and less favorable responses are due to unsuspected factors. The use of concentrated glucose solution, for instance, with ensuing high blood sugar levels may cause acute electrolyte changes within the body and high fever.

The thrilling aspect to me today is to note that more and more of the anuric patients are being maintained in the nonedematous stage. I think up to a year ago I never saw a patient with acute renal shutdown who had not already received too much fluid, and the problem then was complicated by the excess fluid which the patient had been given. I should therefore like to review once again what I consider the three essential phases and the treatment in these three phases.

We have the initial phase, or the phase of injury. It is important for us to realize that while intravascular hemolysis resulting from mismatched transfusions is important etiologically, it is possible to have renal shutdown with nothing more than circulatory failure or shock itself. This is particularly true if one is dealing with elderly patients who already have some diminution in renal function. One must not underestimate what it means for such a patient to have a systolic blood pressure of 50 mm. Hg for an hour or more. An elderly man with some impairment in renal function cannot begin to tolerate the fall in blood pressure which a younger individual can tolerate without resultant oliguria or anuria.

In the initial phase we attempt to prevent the shock from persisting any longer than possible. We try to increase the blood flow to the kidney. If the patient has lost blood, we try to replace blood, but we realize the penalty which will occur if the blood is not most carefully matched.

Where blood is necessary in restoring blood volume in patients immediately and when one is worried in terms of possible hemolysis and ultimate kidney damage, we use washed red cells. If one centrifuges the blood for ½ hour at 3000 RPM, removes the supernatant fluid, washes the red cells, particularly with cold saline, and resuspends the cells in saline or in glucose, one can many times, we believe, diminish the side reactions from whole blood, provided, of course, fresh red cells are used.

If the patient has not lost blood, then plasma, of course, should be used, recognizing again the danger of homologous serum jaundice later if pooled plasma is used. The important point, however, is to minimize the injury from the operative procedure and to restore normal circulation both in volume and pressure.

In the anuric phase, which has been very well discussed by Dr. Leiter, we believe that a liter of fluid per 24 hours is adequate if one is certain that the patient is in fluid balance; in other words, a patient in a good state of fluid balance who undergoes an operation, who develops shock or a hemolytic reaction with a subsequent oliguria or anuria in 24 to 48 hours, and who has been given the routine postoperative fluid therapy, rarely needs additional fluid over and above that required per day. We never use saline (the patient who is anuric, of course, is not losing saline) unless there is a loss of fluid from the gastro-intestinal tract. A rule of thumb is a liter of fluid a day, preferably glucose. If one uses 15 per cent glucose, then one can restore a fair number of calories which keep the endogenous protein breakdown at a minimum.

If the patient is losing fluid in addition or has a high fever or has excessive ventilation, one gives fluid to make up these estimated needs.

Occasionally we use human albumin with our glucose solution. This type of protein does not break down immediately and therefore does not add appreciably to the nonprotein nitrogen or blood urea nitrogen. Albumin and glucose solution should be infused very slowly because of imminent danger of cardiac failure.

There are two immediate sources of potential danger in patients with anuria. One is cardiac, and the other is acidosis. Generally, we digitalize these patients on evidence of any cardiac enlargement. It is a tragedy to lose a patient with renal insufficiency because of cardiac failure. We are not concerned about correcting mild acidosis because, as Dr. Leiter pointed out, the only effective treatment is a sodium salt which will add to the general edema; therefore one must weigh carefully whether the patient's acidosis is severe enough to justify the additional load on the body.

One must not be deceived by a drop in chloride level. If the patient vomits, his chlorides will decrease as a result of this loss. However, he is helping correct his acidosis by this means. One should not give sodium chloride to correct merely a chloride deficit in these patients unless there is a real sodium deficiency.

It is interesting that in most patients with complete anuria, if treated well, the blood urea nitrogen will not rise by more than 12 to 20 mg. per 100 cc a day. If accumulation is more rapid than this, it indicates insufficient glucose calories, continuing hemolysis, or continued infection.

Complete anuria may be tolerated for 7 to 8 days in most instances before one is forced to use accessory procedures.

In the polyuric stage the chlorides often fall very low, particularly since the urine approximates the glomerular filtrate in composition, and hence large quantities of sodium chloride may escape reabsorption by the injured tubule. This represents sodium chloride depletion. During the anuric or oliguric stage we do not give any chlorides. However, as the urine volume continues to increase, evidence of sodium chloride depletion becomes evident, ofttimes with a secondary rise in nonprotein nitrogen and blood urea nitrogen.

In summary, in oliguria and anuria associated with the lower nephron syndrome, care should be taken not to administer excessive fluid and particularly sodium chloride during the anuric or oliguric phase. In the polyuric stage with large volumes of urine and poor kidney function it is imperative to watch patients carefully for evidence of mineral depletion. During this phase it may be necessary to give large quantities of sodium chloride.

Dr. Jacob Fine (Boston, Mass.): I am heartily in accord with virtually everything that Dr. Leiter and Dr. Thorn had to say about the problem of anuria.

I shall confine my remarks to a brief comparison of the Kolff dialyzing machine and peritoneal irrigation. I think it should be obvious to all of you that no one should undertake the treatment of acute renal failure without a thorough understanding of the problem of fluid and electrolyte balance, which are far more complicated than many people realize.

When Dr. Kolff was here last year, I was interested to learn that he had used peritoneal irrigation about as often as he had used his own apparatus and that he thought it was a suitable method in certain situations where he could not use his machine.

At that time it seemed to me at least that the dialyzing machine had many advantages over peritoneal irrigation. Today I am inclined to think the same. However, there are circumstances when the dialyzing apparatus cannot be used; for example, heparinization is sometimes undesirable.

On the other hand peritoneal irrigation as we presented it in a previous publication should no longer be tried, because the danger of peritonitis is too great. We have learned that you should not use the method even with all the changes in detail which we have since developed for greater safety against peritonitis, for more than a very limited period of time, i.e. for not over 60–72 hours. The danger of peritonitis has been considerably minimized. In spite of the fact that of the last 4 patients on whom we have had opportunity to employ the new technique, three recovered, there was peritoneal contamination in one. I am not optimistic about peritoneal dialysis as a practical clinical method until we know more about how contamination of the peritoneum takes place.

Both methods and intestinal lavage deserve thorough clinical exploration of their value and their limitations. I am inclined to think the dialyzing machine will supersede the others, but it is possible that all methods may have their special applications. It is well to remember Dr. Thorn's warning that conservative therapy, intelligently applied will often carry the patient to recovery without the use of these methods.

Dr. Vincent Vermooten (Dallas, Texas): It is a pleasure and a privilege to discuss this paper if for no other reason than to make a plea for the conservative management of renal anuria.

It was in Baltimore on November 10, 1912, and again the following year in Groningen, Holland that Abel, Rowntree and Turner first publically demonstrated the use of their artificial kidney (vividiffusion apparatus). Two years later in their first published report they pointed out, and I think it is extremely important to re-emphasize the point, that the artificial kidney would remove from the blood stream any dialysate which is not present in the solution on the other side of the semipermeable membrane. It is important therefore that the solution used for the dialysis contain dialyzable substances equal in concentration to that already found in the blood stream. If this is not done, then many important electrolytes will be removed from the blood stream. The semipermeable membrane has no specific power of selectivity.

In our own institution, Drs. Grollman, Vanatta, and Muirhead have been engaged for the past year in a study of the artificial kidney as applied to the bilaterally nephrectomized dog. They have found that the procedure, as outlined by Kolff, is subject to innumerable sources of difficulty which may actually prove deleterious to the animal. They feel that the method as recommended for use at present is actually dangerous and not suitable for clinical application. This may explain the discouraging results obtained by Dr. Leiter and his associates.

In analyzing their case reports we find that they used the artificial kidney 7 times in 6 cases. Four of these 6 patients died although case 14 should not rightfully have been included in this group. In the two patients who recovered, the blood urea level was only 110 in case 15 and 109 in case 16. The second time that the artificial kidney was used in case 16, the urea had only risen from 69 to 98 over a 6-day period. In contrast, there were 6 patients all with blood urea levels higher than this who were treated medically with recovery. The patient who had had a bilateral renal decapsulation died 6 days later although at the time of operation the blood urea level was lower than that of most of the successfully treated medical cases.

In the situation we are discussing, we are interested not only in water balance but also in maintaining a correct electrolyte balance. When we realize that this can be very seriously upset by the use of any vividiffusion apparatus, then and only then, it may be safe to use it, otherwise it must be considered an extremely dangerous instrument. There is one further disadvantage in the use of the artificial kidney and that is that each time it is used an artery must be sacrificed.

Although it is well known that renal decapsulation increases renal circulation and although I have always been a strong advocate of early renal decapsulation in cases of anuria, I feel now that it is an unwise procedure unless more evidence can be produced that it does more good than can be counterbalanced by the present regime of treating anuria. The maintenance of a correct fluid balance, prevents edema and so amounts, for practical purposes, to a decapsulation. It must also be remembered, as Blalock has pointed out, that trauma from any operative procedure in itself causes considerable fluid loss as well as a tendency to renal anoxia. Any operative procedure, even decapsulation, would therefore seem to be adding insult to injury.

We have been fortunate, like the authors of this paper, in being able, with few exceptions, to have most of our patients with oliguria due to a lower nephron nephrosis recover when using the general principle of maintaining an adequate fluid balance, by seeing that the patient receives each 24 hours only the quantity of fluid which would be equal to the amount of the previous 24 hour fluid loss (urine, vomitus, etc.) plus 1000 cc for insensible loss and in attempting to maintain a normal electrolyte balance.

Dr. John T. MacLean (Montreal, P.Q., Canada): There are a few points which have been mentioned in Dr. Vermooten's report which I wish to take exception to. We have had a limited experience with the artificial kidney, which you see here—

(Slide)—connected to the patient. Originally we approached it with a great deal of fear and anxiety, thinking that anything might happen. Actually in experience it has proven, once the team was organized and properly coordinated, a very simple matter to operate efficiently and effectively, and I believe, without danger to the patient.

(Slide) This shows the hook-up of the machine. The patient is heparinized before the machine is connected and the machine is heparinized. The blood then circulates through the cellophane tubing, comes out through the pump here. The trap removes the bubbles, and it goes back into the patient.

(Slide) This simply shows the way many of the white blood cells settle out on the colloidal membrane. That is not serious. In the initial phases, there is a drop in the leucocyte count which, after a while is restored to normal.

(Slide) This shows the first patient who was dialyzed, and I think the important thing is to emphasize the fact that the nonprotein nitrogen can be effectively reduced. This patient had prostatic obstruction with acute retention of 4 days' duration. Suprapubic cystotomy was done. He was committed to the artificial kidney room, on his way to the morgue. He was given a dialysis of 3 hours, and the nonprotein nitrogen showed a sharp drop.

Now, this procedure is essentially an arteriovenous shunt and theoretically should be a considerable strain on the circulation. In our limited experience, we have not found it any strain at all. The blood pressure has remained normal, or whatever it was at commencement; likewise the pulse rate has remained normal.

(Slide) I think this is a remarkably interesting case of a boy with a barbiturate poisoning, who became anuric. The machine was applied when his nonprotein nitrogen approximated 200 mg. per cent. Whether it is coincidence or not, I am not prepared to say, dialysis lasted only 1 hour, but it is a fact that the indwelling catheter, once the dialysis was started, produced urine. His nonprotein nitrogen continued to drop and during the next few days returned to normal. He was discharged from the hospital entirely well.

(Slide) This represents a third case of a woman who had a carcinoma of the thyroid, and was admitted to the hospital with abdominal pain. The blood pressure was 250/120. She had a large kidney on each side. Cystoscopy was done and a diagnosis of polycystic kidney disease was made.

Here it was realized that this was not a suitable patient for dialysis, but it was thought if we could tide her over this time, she might go on for a considerable period. She was connected to the machine at that point, when her nonprotein nitrogen was 186. She was carried on for 6 hours. At the 3-hour level we asked her how she felt. She said her head was clear and the foul taste in her mouth was gone. This coincided with a sharp drop in the nonprotein nitrogen.

Dr. Rubin Flocks (Iowa City, Ia.): I have had experience with these cases and a great deal of it has been very satisfactory. Recently in our institution some question has been raised with regard to the use of continuous spinal anesthesia. We have had a good deal of discussion with regard to it. It hasn't been tried, and I should like to ask the previous discussant or the presenters of the paper what they know about it.

Dr. H. Evans Leiter (New York, N. Y.): I want to thank Drs. Thorn, Fine, Vermooten, and MacLean for their very valuable discussion. We bring out the various phases of the treatment of anuria in our paper which could not be read in its entirety due to the limited time.

Our experiences with the Kolff artificial kidney have been similar to those of Dr. MacLean. These cases show definite clinical improvement while connected with the apparatus. We believe that the first 4 patients in whom the machine was used failed to survive because the apparatus was either used too late or the patients were in such severe fluid and electrolyte imbalance that irreversible changes may have occurred within the tissues.

Dr. Kolff advocated the use of a large amount of heparin in dialysis. We have learned by sad experience that such large doses are unnecessary. With the last 3 artificial kidney "runs", we have used a total of 250 mg. heparin for a 6-hour dialysis, and during this time we have had no trouble whatsoever with excessive coagulation of the blood.

We have had very little experience with peritoneal lavage. Dialysis in general is an important adjunct in the treatment of acute uremia and we know that simpler machines will be or have been devised for dialysis.

In conclusion, I wish to state that the successful management of renal insufficiency depends upon the capacity of the kidneys to recover adequate function and on our ability to maintain artificially within physiological limits the various functions normally carried out by the kidneys. The artificial kidney is a safe and valuable adjunct in the treatment of acute uremia and is best used while the patient is still in fair condition and the blood urea or nonprotein nitrogen levels are only moderately elevated.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

ADDISONIAN CRISIS PRECIPITATED BY NEPHRECTOMY[1]

JOSEPH J. KRISTAN

From the Veterans Administration Hospital, Coral Gables, Fla.

Adrenal cortical insufficiency (Addison's disease, hypoadrenalism, hyposuprarenalism) has been thoroughly described in the literature. Articles discussing the protean nuances of the clinical picture[2, 3] and the various diagnostic procedures[4, 5, 6, 7] with modifications[8, 9] are numerous. Very few reports have stressed the need to consider the possibility of a co-existent adrenal tuberculosis in cases of urogenital tuberculosis, especially in any case in which surgical treatment is contemplated. This paper presents a case of latent tuberculous adrenal cortical insufficiency in which the clinical course following nephrectomy made the diagnosis manifest.

CASE REPORT

A white man, aged 37, was admitted on April 28, 1947 with the chief complaints of weakness, dizziness on changing positions, and headaches with nausea. His past history revealed that weakness and loss of energy had *begun insidiously* in 1941, six months after enlistment in the Army. Several basal metabolism rate determinations were made (minus 25 and minus 31) and resulted in the presumptive diagnosis of hypothyroidism. Two grains of thyroxin daily gave but slight benefit. At that time a left varicocele and a skin condition, termed eczema, were present. Because of this skin condition he was given a medical discharge in April 1943. Following discharge, his symptoms continued but he was able to do mild physical work. There was occasional matutinal nausea without emesis and he noted a transient dizziness in suddenly changing from the recumbent to erect position. He consulted a physician who continued the thyroxin treatment and gave liver injections for anemia. At this time the patient volunteered the information that he had noticed pink seminal fluid on several occasions. Further investigation revealed an enlarged left kidney, and after guinea pig inoculation, the diagnosis of tuberculosis of the left kidney was made. Slight frequency was the only urinary symptom.

---

[1] Published with the permission of the chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

[2] Rowntree, L. G. and Snell, A. N.: A Clinical Study of Addison's disease. Philadelphia: W. B. Saunders Co., 1931.

[3] Conn, J. W. and Mathews, K. P.: Addison's disease in the Negro. Am. J. M. Sc., **212**: 404–409, 1946.

[4] Siglin, I. S.: Addison's disease, a diagnostic problem: Report of a case. Proc. Staff Meet., Mayo Clin., **22**: 17–24, 1947.

[5] Robinson, F. J., Power, M. H. and Kepler, E. J.: Two new procedures to assist in recognition and exclusion of Addison's disease; preliminary report. Proc. Staff Meet., Mayo Clin., **16**: 577–583, 1941.

[6] Schneider, R. W.: Appraisal of water test of adrenal function. Cleveland Clin. Quart., **11**: 22–25, 1944.

[7] Willson, D. M., Robinson, F. J., Power, M. H. and Wilder, R. M.: Diagnosis of Addison's disease; further experience with Cutler-Power-Wilder sodium chloride restriction test. Arch. Int. Med., **69**: 460–469, 1942.

[8] Thorn, G. W.: Diseases of the Adrenal Gland, in A Textbook of Medicine by Cecil, R. L. Philadelphia: W. B. Saunders Co., 1947, p. 1365.

[9] Albrecht, F. K.: Modern Management in Clinical Medicine. Baltimore; Williams & Wilkins Co., 1946, p. 635.

In April 1945 a left nephrectomy was performed. Preoperatively, 2 pints of blood were given, raising the red cell count from 3,890,000 to 4,490,000. The blood pressure was 124/82. The operative and immediate postoperative condition was satisfactory. Ten hours after operation the blood pressure began to drop (80/60) and a 500 cc blood transfusion, glucose and saline, and adrenalin were given. The blood pressure remained lowered and the next day another pint of blood was given and, since adrenal insufficiency was suspected, cortical extract (cortate) 10 mg. statim and 5 mg. every 6 hours was given. Gradually the pressure rose to 90/50 but the patient appeared very ill, vomiting moderately. Severe abdominal distention responded well to vigorous treatment with prostigmine, intubation, gastric lavage and infusions. The nonprotein nitrogen was 64.7 mg. per cent; the plasma chloride, 630 mg. per cent (saline infusions had been given); and the red cell count, 3,680,000. On the third postoperative day there was marked atelectasis of the right lung. Daily infusions of glucose and saline were continued and the cortical extract dosage gradually reduced to 5 mg. each day. A total of 3 pints of blood were given postoperatively with a resultant red cell count of 3,690,000. The nonprotein nitrogen value returned to normal on the fifth day. After 2 weeks the patient was still quite weak but was discharged to his home without further cortical extract therapy. The pathological diagnosis was ascending tuberculous pyelonephritis.

During the 3 days following discharge, the patient became progressively weaker and was returned to the hospital in collapse. The systolic pressure was between 60 and 70 mm. Hg. Ten milligrams of cortate and salt, in amounts up to 9 gm., were given daily. The blood pressure ranged between 70 and 120 mm. Hg. and upon discharge cortate (7 mg. daily) was continued.

In June 1945 he was referred to a physician for confirmation of the diagnosis of Addison's disease. Physical examination revealed a 5 foot 5 inch tall, 110 pound patient who appeared to be chronically ill. The blood pressure was 95/60 and the pulse 72. The skin and oral mucous membranes were somewhat pale but without unusual pigmentation. The thyroid gland was normal in size. The examination of the heart, including fluoroscopy and electrocardiogram, was negative. A small left varicocele was present. The reflexes were hyperactive and equal. Laboratory data: red blood cells 3,900,000; hemoglobin, 12.5 gm.; and fasting blood sugar, 110.7 mg. per cent. The Kepler water test[4, 5] was positive in both parts. In part 1[10] the largest hourly diurnal volume was 134 cc. and the total nocturnal volume 170 cc. Part 2 revealed A to be 23.5 (plasma urea nitrogen, 10.0 mg. per cent; urine urea nitrogen, 657.0 mg.

---

[10] If, in part 1, the volume of the largest hourly specimen voided in the morning is less than the total nocturnal volume, the response to the test is positive: Addison's disease may or may not be present.

If, in part 2, A $\frac{(\text{mg.\% urea (urine)})}{(\text{mg.\% urea (plasma)})} \times \frac{\text{mg.\% chloride (plasma)}}{\text{mg.\% chloride (urine)}} \times \frac{\text{volume day urine}}{\text{volume night urine}}$ is less than 25, the patient probably has Addison's disease, provided nephritis has been excluded. If A is greater than 30 the patient probably does not have Addison's disease.

per cent; plasma chloride, 526.1 mg. per cent; and urine chloride, 1157.5 mg. per cent). Abdominal x-ray revealed bilateral adrenal calcification. Seven and one-half milligrams of desoxycorticosterone acetate (DOCA) and supplemental salt were given daily. A great improvement was noted and the patient's weight increased to 135 pounds.

In July 1945 fifteen pellets[8, 11] of desoxycorticosterone acetate (percortin, each pellet containing approximately 125 mg.) were implanted with good results. After 1 year his former symptoms returned and he was given oral adrenal cortical extract (glycortal) and 6 to 9 gm. of salt daily. This treatment was much less satisfactory.

Upon admission to this hospital he again complained of weakness, enervation, anorexia, drowsy spells, morning nausea, transient dizziness upon changing from the prone to upright position, and frontal headaches which were relieved by walking. Libido and potentia were decreased. No weight loss had been noted. There was no history of drug intake. The family history revealed maternal pulmonary tuberculosis years previously and there had been close contact with the patient. Repeated x-ray examinations of the patient had been negative. Prior to the onset of symptoms in 1941 the patient had enjoyed fine health, having had no serious illnesses.

Physical examination was essentially the same as previously noted. There was no abnormal pigmentation, the body weight was 137 pounds, and the blood pressure when prone was 86/60 and when erect 60/40. The basal metabolism rate was minus 32 and upon another occasion, minus 28. A chest film revealed a normal cardiothoracic ratio and an electrocardiogram was normal. Calcification of the right adrenal gland was shown by x-ray. A gallbladder series revealed many fine stones. A 5-hour glucose tolerance test done at 1-hour intervals gave values of 90, 97, 90, 55, 93, and 80 mg. per cent. The red cell count was 4,090,000, the hemoglobin was 13 gm. (Hadenhauser), and the Kahn test, white-cell count and urinalysis were normal. A phenolsulphonphthalein test showed 28 per cent dye excretion after 2 hours and a blood urea nitrogen was 13.1 mg. per cent. A urine culture was negative for tubercle bacilli. The Kepler water test was positive in both parts. In part 1 the largest hourly diurnal volume was 100 cc and the total nocturnal volume 240 cc. Part 2 revealed A to be 4.57 (plasma urea nitrogen, 6.5 mg. per cent; urine urea nitrogen, 220 mg. per cent; plasma chloride, 512 mg. per cent; and urine chloride, 1580 mg. per cent).

Moderate improvement was noted with 5 mg. DOCA and 4 gm. of salt daily. The morning headaches continued as did a slight degree of lassitude. The blood pressure ranged between 90/65 and 155/110. Following stabilization and determination of extract requirements, nine pellets of percortin (each pellet containing approximately 75 mg.) were implanted, and supplemental salt was given daily. He was discharged and was to return in 3 months.

---

[11] Thorn, G. W. and Firor, W. M.: Desoxycorticosterone acetate therapy in Addison's disease; clinical considerations. J. A. M. A., 114: 2517–2525, 1940.

DISCUSSION

Although this patient had symptoms compatible with early adrenal cortical insufficiency for almost 4 years, the diagnosis was not suspected until after nephrectomy. The manifestation of acute transient or permanent adrenal insufficiency has been reported following acute infections,[12] pregnancy[13] and surgical procedures.[14, 15] In our case the presence of renal tuberculosis helped to obscure an underlying adrenal insufficiency. Rowntree and Snell[16] have emphasized the fact that a complicating disease may mask the diagnosis and stated that in 8 cases of a series in which latent or atypical adrenal insufficiency was present, surgical procedures precipitated a fatal outcome. In 1933 Greene, Walters and Rowntree[17] stressed the clinical importance of considering fully the possibility of suprarenal tuberculosis with latent Addison's disease as a complication among patients who present themselves for the surgical treatment of tuberculosis of the urogenital tract. They reported that in only 1 of 6 such cases was the possibility of Addison's disease suspected prior to operation. In all the cases extensive caseous tuberculosis of both adrenal glands was found at necropsy. The diagnostic implications are as pertinent today but fortunately errors in diagnosis are often of less consequence now that the physician has an improved armamentarium to cope with such distressing and formerly fatal postoperative developments. Boyd[18] reported a fatal case following orchidectomy for tuberculosis and in the discussion which followed the presentation, 2 physicians spoke of rather similar cases and agreed that the diagnosis is easily missed. The paucity of similar reports may well be explained by the natural reluctance to publicize one's errors. Relative to the possibility of operative damage to the adrenal gland as a precipitating factor, Kaufman,[18] in reviewing 50 cases of nephrectomy in 1936, brought out the fact that little attention has been given to it in the literature. He believed that it was far more common than suspected and that the accidental injury to the blood and nerve supply of the adrenal gland constituted an important cause for immediate and remote evidences of shock after nephrectomy, usually however attributed to other factors. In the mobilization of the upper pole of the kidney and in the application of the clamps there is real danger of injuring the gland. In the series reviewed he reported 4 cases with postoperative collapse, in 2 of which a portion of the adrenal gland was accidentally removed, resulting in death in 1 patient. In 2 others collapse without hemorrhage occurred and the role of the adrenal was brought into consideration. In one a transient hypertension (208/130) was followed by a persistent hypotension (75/65) which was finally alleviated by cortical extract (eschatin). Wildbolz[19] and Walters[20] advise the very careful separation of the perirenal fatty capsule from the kidney before elevating the latter out of the incision. Wildbolz discussed 2 cases, both with past histories of tuberculosis, in which death occurred following nephrectomy for tuberculosis of the kidney and he incidentally mentioned three possibly similar cases seen by his confreres. A fatal case in which the adrenal gland was unintentionally removed with the kidney, was recorded by Beer and Hyman.[21] Goldstein[22] related the case of hemorrhage from an adrenal vessel following the removal of one-half an adrenal gland during nephrectomy. Harrison and Pote[23] mention a case in which, during the removal of a kidney badly damaged by infection and pressure, a part of the adrenal gland was caught in a pedicle clamp and removed. Acute adrenal insufficiency followed, was treated with DOCA, and after 26 days recovery was complete, requiring no further treatment. Cases have been presented, however, in which the removal of a single caseous adrenal gland, or even bilateral partial resection of the glands, resulted in no clinical evidence of insufficiency. This is compatible with the comments heard that approximately 80 per cent of the tissue must be nonfunctioning before symptoms appear. Perhaps in some cases where insufficiency transiently appears without the removal of much or any of the gland, the presumption of a temporary post-traumatic reflex shutdown is plausible.

---

[12] Robbins, J. H.: Use of cortin in a cas [illegible] occurring as a sequela of acute streptococcic sore throat.

[13] Sheldon, D. E.: Pregnancy complica [illegible] m. J. Obst. & Gynec., 49: 269–272, 1945.

[14] Leavitt, P.: Crisis in Addison's disease precipitated by acute appendicitis. New York State J. Med., 45: 1987–1989, 1945.

[15] Laipply, T. C.: Addison's disease due to cytotoxic contraction of adrenal cortex with sudden death 4 days after appendectomy. Ohio State M. J., 39: 652–653, 1943.

[16] Snell, A. M. and Rowntree, L. G.: Clinical experience with Addison's disease. Ann. Int. Med., 3: 6–28, 1929.

[17] Greene, C. H., Walters, W. and Rowntree, L. G,: Surgical operations in Addison's disease, successful epididymectomy and orchidectomy for tuberculosis. Ann. Surg., 98: 1013–1017, 1933.

[18] Kaufman, L. R.: Complications and accidents of nephrectomy. Urol. & Cutan. Rev., 40: 302–308, 1936.

In reviewing the literature one is unduly impressed with the danger associated with the Wilder provocative test[7, 24] of adrenal insufficiency. Most articles consistently refer to 2 cases[25,26] only, in which death presumably resulted. Upon reading the case reports it appeared that clinically the test was contraindicated in both and in one[25] was prolonged excessively. In the other case the author commented: "Sudden death is common in Addison's disease and its occurrence here may have been entirely fortuitous." The diagnosis of adrenal cortical insufficiency cannot be reduced to a mathematical formula and laboratory tests must be used discriminately and they cannot serve as a substitute for diagnostic acumen which can only result from careful clinical study and experience. Clinical judgment used in the evaluation of the signs and symptoms in conjunction with the results of selected necessary laboratory tests will usually result in the correct diagnosis without undue risk to the patient. In cases with little objective evidence of Addison's disease but with many subjective symptoms one may usually use the Wilder test with little danger as a test of exclusion.[8]

---

[19] Wildbolz, E.: *Nebennierentod* nach Nephrektomie wegen Tuberkulose. Ztschr. f. urol. Chir., 39: 72–77, 1934.

[20] Walters, W.: Personal communication.

[21] Beer, E. and Hyman, A.: Progress in nephrectomy, a study based on a series of 207 cases. J. A. M. A., 75: 1180, 1920.

[22] Goldstein, A. E.: *Accidents in renal surgery.* Surg., Gynec. & Obst., 65: 515–522, 1937.

[23] Harrison, F. G. and Pote, H. H.: Postoperative adrenal insufficiency. J. Urol., 45: 315–321, 1941.

[24] Cutler, H. H., Power, M. H. and Wilder, R. M.: Concentrations of chloride, sodium and potassium in urine and blood; their diagnostic significance in adrenal insufficiency. J. A. M. A., 111: 117–122, 1938.

[25] Garvin, C. F. and Reichle, H. S.: Death presumably due to use of salt restriction test in diagnosis of Addison's disease. Ann. Int. Med., 14: 323–324, 1940.

[26] Lilienfeld, A.: Use of low salt diet in diagnosis of Addison's disease. J. A. M. A., 110: 804–805, 1938.

SUMMARY

A case of latent adrenal cortical insufficiency, which was diagnosed and treated only after nephrectomy for renal tuberculosis, is presented.

Concurrent complicating diseases may mask the diagnosis of cortical insufficiency.

The possibility of a latent or atypical adrenal cortical insufficiency should be considered in all cases of urogenital tuberculosis, especially in those in which surgical treatment is contemplated.

The Journal of Urology
Vol. 61, No. 2, February 1949
Printed in U.S.A.

SULFATHIAZOLE ANURIA CURED BY MEANS OF INTRAVENOUS PROCAINE TREATMENT[1]

NIELS PEER FRIIS

> "Emergency decapsulation in severe cases associated with the syndrome is more urgent than appendectomy in acute appendicitis . . ."
>
> *Johan T. Peters*

As is known, acute anuria is a severe complication in several disorders[3, 8], and the most effective treatment has proved up to now to be an early bilateral decapsulation[2, 7] with a simultaneous, moderate restriction of the fluid intake in order to avoid interstitial edema and increased intrarenal pressure[5, 7]. The following case record and the reference to 3 similar cases[3, 4, 6], however, indicate a new form of therapy which, it is to be hoped, may prove effective, despite its simplicity, in most cases of acute anuria.

The case is that of a woman, aged 31 years, who was treated for bronchopneumonia (October 1946) with *sulfathiazole, being enjoined, as are all patients,* to drink much during this treatment. She was previously always in good health, apart from repeated attacks of Quincke's edema. After the administration of 15 gm. sulfathiazole she had nausea and vomiting, and anuria (catheterization proved the bladder to be empty). Anuria had been present for 23 hours when a trial dose of 5 cc of 1 per cent procaine hydrochloride solution was given slowly in intravenous injection (75 seconds). Hypersensitivity was guarded against by measuring the pulse and the blood pressure, and soon after a therapeutic dose of 10 cc of 1 per cent procaine hydrochloride solution was injected intravenously in the course of 150 seconds. Two and one-half hours later the patient passed a small portion of sanguineous urine, with lancinating pain radiating from the renal regions along the ureters and down towards the bladder; once the diuresis had been started again, the patient passed a total of 250 cc urine in the course of the next 16 hours (15.6 cc/hour) with frequent micturition. In order to bring about a further increase of the diuresis, another 10 cc procaine was injected, producing an increase to 78 cc/hour, and 4 hours later still another 10 cc procaine, increasing the diuresis to 112.5–159.4–177.8 cc/hour, so that during the first 48 hours the quantity of urine excreted was respectively 1,012 cc (+ albumin, + blood) and 3,850 cc (no albumin, no blood). Table 1 is a graphical representation, the abscissa being the time stated in hours, and the ordinate representing the diuresis in cubic centimeters per hour. In the course of a week the blood urea decreased from 123 mg. per cent to normal (23 mg. per cent).

---

[1] Read before the Dansk Selskab for intern Medicin, November 1946.

[2] Abeshouse, B. S.: J. Urol., 53: 27–84, 1945.

[3] Friis, N. P.: XX nordiske Kongres for intern Medicin, Gothenburg, June 1946. (To be subsequently published in Acta med. Scandinav.)

[4] Langeron, L., Paget, M. and Michaux, P.: Bull. et mém. Soc. méd. d. hop. de Paris, 62: 58, 1946.

[5] Lattimer, J. K.: J. Urol., 54: 312–318, 1945.

[6] May, Netter and Gerbaux: Société Médicale des Hôspitaux, 1943.

[7] Peters, J. T.: Ann. Int. Med., 23: 221–236, 1945.

[8] Peters, J. T.: Acta med. Scandinav., 123: 90, 1945.

During the entire course the patient was treated with pulvis natrii bicarbonatis and, in spite of great thirst, her fluid intake was moderately restricted, the total quantity being 1,300 to 1,500 cc a day. In the meantime the pneumonia had been treated with penicillin, and on the seventh day the patient was for the first time in complete well-being. She had a good appetite, the blood urea being normal at the same time, the diuresis and the amount of fluid ingested also balancing. After 10 days in bed she had recovered completely. On subsequent examination the x-ray of the urinary tract showed nothing abnormal. See figure 1.

According to anamnesis and case history, this is probably a case of acute anuria on a mixed pathological basis, toxic (allergic and incrustation) producing. Table 1 shows the increase of diuresis in direct connection with the intravenous injections of procaine: from complete anuria to 1) 15.6, 2) 78.0 and 3) 112.5 and on to 159.4 and maximum 177.8 cc per hour.

TABLE 1

1ST DAY: ANURIA	2ND	3RD	4TH	5TH	6TH	7TH
Blood urea, mg. %......	111	123	71	80	41	23
Diuresis, cc............	1,012	3,850	2,460	1,910	1,610	1,550

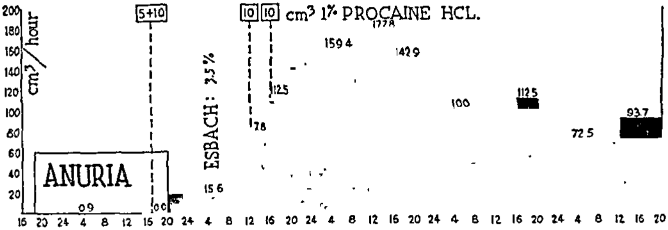


FIG. 1

The administration of sodium bicarbonate does not only aim at increasing the solubility of sulfathiazole (which, as is seen, was not materially changed), but is also intended to produce a tissue reaction[6], which is more capable of obviating the imminent injuries to the parenchyma. The moderate restriction of the fluid intake is of importance in the further course as well as in the acute stage, since by overcharging the impaired kidneys we run the risk of secondary insufficiency with increasing uremia[7].

The effect of the procaine treatment must be supposed to be due to a transient blocking of the symphathetic, perhaps with a direct action on the renal functions[3]. The treatment is contraindicated in case of cardiac disorder with disturbances of conduction. Owing to the easy administration it will be therapy which, instituted as soon as possible and as often as required, should not be left untried before we proceed to a possible decapsulation.

This method of treatment was first employed by the French clinicians May, Netter and Gerbaux[6], one of their patients having developed intoxication with anuria in the course of treatment with arsphenamine. The anuria had persisted for 20 hours when intravenous procaine treatment was instituted, and 1 hour afterwards the diuresis had been started. I previously have treated a case of anuria calculosa[3] of 48 hours' standing which was obviated 1 hour after injection of procaine. Lastly, a case has recently been reported by Langeron, Paget and Michaux[4]; this was also a case of sulfathiazole anuria, in which the diuresis was started after 12 injections of procaine, given every 2 hours.

Addendum: Since the manuscript was prepared, the important work by Trueta and co-workers: *Studies of the Renal Circulation*, Oxford, 1947, has appeared, and I would draw attention to a comparison between my examinations of the effect of procaine on experimental vasopressinogen anuria (*Acta Medica Scandinavica*, supplement 206, p. 236: In Water metabolism tests with 1.5 litres, 5 healthy young men had injections of 30 i.u. vasopressin with subsequent anuria for about 4 hours; the anuria was reduced by about 1 hour after intravenous injection of 10 cc. of a 1 per cent procaine-hydrochloride solution, other things being equal) and the proofs, as given by Trueta in chapter 3, of the influences of vasopressin and the adrenergic substances on the renal circulation as being a readjustment to the juxtamedullary glomeruli.

Copenhagen, Denmark

THE JOURNAL OF UROLOGY
Vol. 61, No 2, February 1949
Printed in U S A.

UNILATERAL MULTIPLE CYSTS OF THE KIDNEY[1]

CHARLES P. HOWZE AND JOHN H. HILL

In 1944, Braasch and Hendrick proposed the following classification of renal cysts: 1) retention or inflammatory cysts; 2) simple cysts—single, multiple, multilocular and hemorrhagic; 3) peripelvic (pyelogenic cysts); 4) parapelvic cysts; 5) cysts secondary to renal pathological changes (calculus, hypernephroma, tuberculosis, pyelonephritis, hematoma and ecchinococcus); and 6) polycystic kidneys.

We wish to report 2 cases of unilateral polycystic kidney. The term polycystic is used to denote multiple discrete cysts of the kidney and not multilocular cysts, which are large cysts subdivided into multiple smaller divisions.

The reported cases of unilateral cystic disease are few in number. In 1933 Braasch and Meland presented 10 cases of multilocular cysts of the kidney in adults and in 1944, Braasch and Hendrick added 2 similar cases. Six cases have been reported in children. The 2 cases in this communication bring the total to 8. The unilaterality of renal cysts is open to controversy. Clinically there are only 2 ways of determining accurately their presence: 1) by pyelographic studies and 2) inspection and palpation of the kidney on the operating table. Either method could fail to discover minute cysts. In spite of this fact, we believe that unilateral cysts do occur as do other unilateral congenital anomalies of the upper urinary tract. In a study of the reported cases in infants and children (table 1) it is noted that 4 are reported as multicystic (discrete cysts) and 4 as multilocular. A pertinent observation in the first group was the absence or incomplete development of the primodial renal arteries, collecting tubules, calyces and pelvis; namely the lateral segmental branch of the dorsal artery and the metanephric diverticulum. The age of the youngest patient in this series was 20 days and the oldest 13 years. There were 6 males and 2 females; 1 Negro and 7 white. The predominating sign in the infant cases of unilateral cystic kidneys has been a mass in the region of the kidney. Hematuria was observed in 2 cases. In 6 instances, the mass was on the left and in 2 on the right. Except for an occasional pus cell in 2 cases, the urinalyses were normal. Seven cases were treated by nephrectomy and later reported cured. Campbell's case was found at autopsy.

Many explanations for renal cysts have been advanced. Hildebrant's belief that cyst formation results from failure of union of the nephroblastemic elements (glomeruli) and the collecting tubules was accepted for years, but other experimental studies have offered interesting speculation. Kampmeier shows a separate origin for the convoluted and collecting tubules of the kidney. In a study of fetal kidneys he found that there is a period of fetal development characterized by the existance of cystic renal tubules. Normally this generation of tubules collapse and disappear. However, the persistence of these is thought

---

[1] Read at annual meeting, American Association of Genito-Urinary Surgeons, Skytop, Pa., May 14, 1948.

TABLE 1

CASE REPORTS	AGE	SEX	SIGNS AND SYMPTOMS	SIDE	PATHOLOGICAL FINDINGS
1. Schwartz	7 mos.	M	Mass	Left	Multicystic: No definite renal artery, pelvis, calyces, pyramids or cortex. Pea-size renal tissue; nonfunctioning
2. Lynch and Thompson	7 mos.	F	Mass	Left	Multicystic: Condition of renal artery and pelvis not stated in report. No normal renal tissue
3. Howze and Hill (Case 1)	20 days	M	Mass	Left	Multicystic: Minute renal vessel at upper pole. Small ureter but no definite renal pelvis or calyces. No normal renal tissue
4. Howze and Hill (Case 2)	13 yrs.	M (Negro)	Pain RLQ hematuria	Right	Multicystic: No renal artery or pelvis noted. No functioning renal tissue
5. Dakin	2 yrs.	F	Pain and mass	Left	Multilocular: No renal pelvis, ureter or calyces. No urogram and no histological report given
6. Campbell (Autopsy Case)	4 wks.	M	History not reported	Right	Multilocular: No pelvis or calyces; ureter impervious. No histological report given. Left kidney normal
7. Burrell	3 yrs.	M	Mass and hematuria	Left	Multilocular: Renal pedicle normal. Island of cysts at lower pole; surrounded by functioning renal tissue
8. Toulson and Wagner	19 mos.	M	Mass	Left	Multilocular: Renal pedicle normal. Cysts circumscribed by functioning renal tissue

to be the origin of renal cysts. Virchow thinks cystic formation results from obstruction of the papillary ducts by urinary salts or inflammation, but Patterson has shown the obstruction results in tubular atrophy Hinman and Morison found that fetal renal circulation persists in the polycystic kidney and that the finer vessels of the cortex are compressed and displaced Hepler notes that interference with the intraparenchymal blood supply leads to cystic degeneration in the involved area He later produced a large solitary cyst of the kidney by ligating the posterior branch of the renal artery and simultaneously fulgurating the papilla of a rabbit's one lobed kidney His experimental data offer an insight to the understanding of the pathological observations in these cases of renal cysts in children The location, degree and duration of the disturbance with the renal blood supply seem to govern the extent of renal tissue degeneration In the 4 multicystic cases, normal renal tissue was inadequate or noticably absent In the multilocular cystic case of Toulson and Wagner and that of Burrell, there was intrarenal vascular compression, but, functioning renal tissue was present as evidenced by excretory urograms No histological study was reported in Dakin's and Campbell's cases In the case of our 13 year old Negro boy, the kidney was found in an ectopic position and no true renal artery was found Functioning renal tissue was apparently inadaquate as shown by its failure to excrete dye in the urogram

The presence of a renal cystic mass at birth in these infant cases proves their congenital origin The fetal arrest in the development of the renal artery and pelvis, as evidenced by the pathological findings in many of the operative specimens, seems to influence the formation of cysts and the diminution of the functioning renal tissue

CASE REPORTS

Case 1 J P , an infant white boy aged 14 days, entered Childrens Hospital May 13, 1947 A routine post-delivery examination revealed a mass in the left side of the abdomen, and the absence of the left testicle from the scrotum No other abnormality was found There was a history of a normal delivery This was the first child and there were no miscarriages

Physical examination showed a well developed, bottle fed infant, weighing $8\frac{1}{2}$ *pounds* He was *apparently not acutely ill* The head, neck and chest presented no abnormalities The abdomen was soft and distended There was a globular, nontender, slightly movable mass filling the entire left side of the abdomen The liver was palpated two finger breadths below the costal margin

A plain film of the abdomen showed the presence of a soft tissue mass occupying the left flank and displacing the stomach upwards and the intestines to the right The mass appeared to be the size of an orange Excretory urograms, after subcutaneous injection of diodrast, revealed the presence of dye in the right kidney but none on the left After 10 minutes the calyces and pelvis on the right were faintly outlined and appeared normal At the end of 30 minutes the right kidney was emptied but still no dye was seen on the left The bladder appeared normal in size and contour A gastro intestinal x-ray study was reported normal

Urine· clear, specific gravity not (sufficient quantity), reaction, acid, albumin and sugar, negative; microscopic: 6–10 pus cells per high power field. Red cell count: 5,500,000; white cell count 7,400; hemoglobin 17.5 gm.

The possibility of a Wilms' tumor was considered and surgical exploration was advised.

A transverse incision was employed, beginning 2 cm. above the umbilicus and extending to the left lumbar region midway between the lower ribs and iliac crest. The peritoneum was opened and the right kidney was palpated and found normal in size and free of cysts on its surface. The intestines and stomach were retracted to the right. Behind the posterior peritoneum was a multicystic mass extending from under the diaphragm to the pelvic brim. The posterior peritoneum was incised over the cystic tumor. The tumor consisted of multiple cysts varying in size from a golf-ball to a small grape. No renal tissue was apparent. The mass was freed from the surrounding tissue and found attached to a normal size ureter. On the lateral border of the mass was found the left testicle, which was removed with the tumor after severing ligaments at each pole of the testicle. Only one small vessel was ligated near the upper portion of the cystic mass. The wound was closed in the conventional manner. Postoperative course was uneventful and the baby left the hospital 2 weeks following operation (fig. 1).

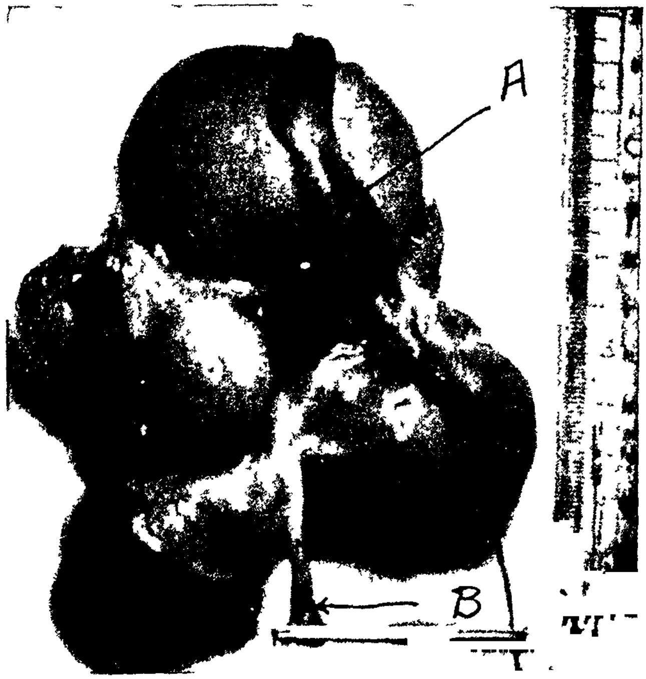


FIG. 1. Multiple cysts replacing kidney. *A*, testicle; *B*, ureter

The specimen consisted of a transparent multicystic mass measuring 18 by 7 by 6 cm. There was no apparent functional renal tissue present. Five centimeters of the ureter was attached to the specimen. Aspiration of the cysts showed a golden clear fluid. The wall of the cysts was about 1 mm. in thickness. There was a small piece of testicular tissue present. The position and ligamentous attachments of the testicle are embryologically understood. In the human embryo the gonadal ridge is on the ventral border of the mesonephros. The evanescent mesonephric tubules later become the diaphragmatic ligament. This ligament and the inguinal ligament were found attached to the upper and lower poles of the testicle respectively. Sections of the cysts showed a connective tissue wall lined by a thin layer of cuboidal to flat epithelial cells, sharply defined from sub-epithelial structures. Scattered blood vessels were also seen. There was no evidence of malignancy in this specimen. Sections of the testicle consisted of well differentiated, rather congested and atrophic testicular tissue. There was nothing suggestive of neoplasm or any other specific pathological process. Diagnosis: Congenital multicystic kidney; atrophic testicle.

Case 2. C. M., a Negro boy, aged 13 years, was admitted to Garfield Memorial Hospital June 19, 1940, complaining of fever, chills and sweats for a period of 3 weeks. There had been some pain in the lower right quadrant, but he had had no nausea or vomiting. The past history disclosed hematuria on several occasions not accompanied by other urinary signs or symptoms.

Physical examination revealed a well nourished, well developed Negro boy, apparently ill. There was tenderness in the lower right quadrant of the abdomen, associated with some rebound tenderness. No mass or muscle splinting was noted. A mitral murmur and accentuated pulmonic second sound were found on heart examination. The blood pressure was 120 systolic and 62 diastolic. The external genitalia and rectal examinations were normal.

The urine was normal except for a trace of albumin. Blood urea: 32 mg. Red blood count 3,420,000; white blood count 6,050; hemoglobin 57 per cent. The blood calcium was 10 mg. and the inorganic phosphorus 2.7 mg. per 100 cc. The Wassermann and Kahn reactions were negative. Blood smears for malaria were positive for Plasmodium vivax on 2 occasions. The phenolsulphonpthalein was excreted in the following concentration: after 15 minutes, 50 per cent; 30 minutes, 9 per cent; 60 minutes 12.5 per cent; total 71.5 per cent.

A flat film of the urinary tract revealed both psoas outlines to be fairly distinct. There were no shadows suggestive of urinary calculi. The left renal shadow was identified but the right was not seen. Intravenous pyelograms revealed a normal left kidney pelvis. X-ray exposures at 3, 5, 5½ and 7 hours failed to show any dye excreted by the right kidney.

Cystoscopy was performed to determine the cause of hematuria. The bladder was normal and the ureteral orifices were normal in size, shape and position. A No. 5 ureteral catheter was passed easily to the left kidney and normal urine was obtained. On the right side the catheter was obstructed at the 10 cm. marking. No urine was obtained from this side. A left retrograde pyelogram was made and found to be normal. The right catheter was injected with skiodan, which regurgitated into the bladder without delineating a right renal pelvis (fig. 2).

Operation was performed through the usual lumbar incision. There was no kidney in the lumbar fossa. After considerable search, a small multicystic mass, about the size of small oyster, was found in the iliac fossa. It was loosely attached to the peritoneum. No definite renal pedicle was apparent. The cystic mass

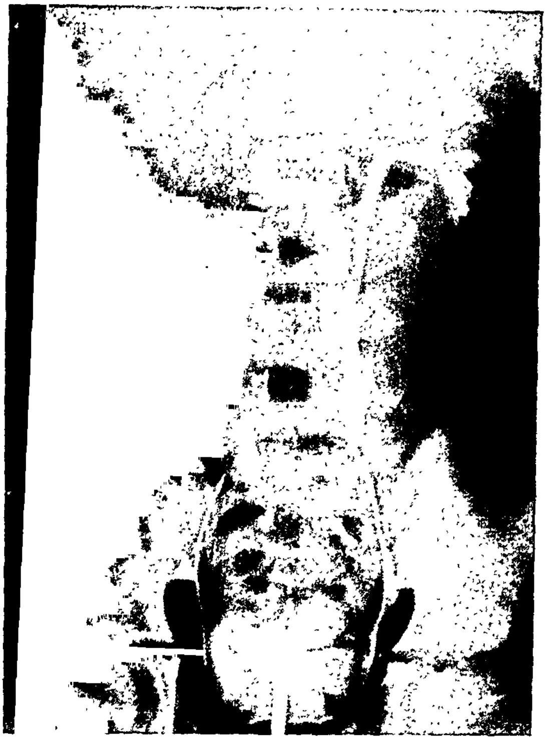


FIG. 2. Normal left pyelogram. Right catheter obstructed at 10 cm.

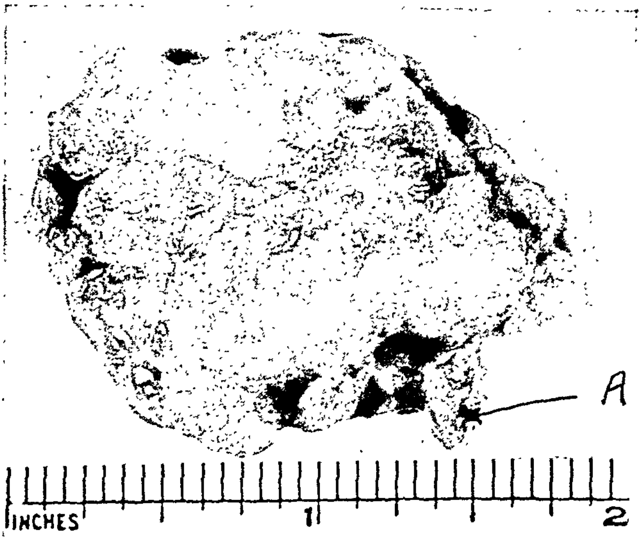


FIG. 3. Multiple cysts of congenital atrophic kidney. *A*, Ureter

was attached to a small ureter which was divided and ligated. The wound was closed in layers. The postoperative course was uneventful and the patient was discharged from the hospital in 12 days following operation.

The specimen consisted of a cystic mass weighing 18.5 gm. and the portion of the ureter measuring 2 cm. The capsule appeared injected and showed beneath its surface numerous cysts, averaging 5 mm. in diameter. A small amount of perirenal fat was attached (fig. 3). The sections of the kidney showed, between the cystic areas, dense fibrous tissue and thick walled blood vessels and on occasional tubule occurring singularly and in small groups. In some instances they contained homogenous pink staining material. Calcium granules were occasionally seen. Diagnosis: Multicystic kidney with fibrosis.

CONCLUSIONS

One case of unilateral multicystic kidney in a 20 day old boy and 1 case of unilateral multicystic kidney in a 13 year old boy are presented. Similar cases collected from the literature are reviewed.

The clinicopathological finding of absence or incomplete development of renal artery and pelvis in children, concomitant with retardation of the renal tissue growth and cyst formation, lends added significance to Hepler's laboratory experiments.

1150 Connecticut Ave., Washington, D. C.

REFERENCES

Braasch, W. F. and Hendrick, J. A.: J. Urol., 51: 1–10, 1944.
Burrell, N. L.: J. Urol., 43: 656–663, 1940.
Campbell, M.: Pediatric Urology. New York: Macmillan, 1937, vol. 1, p. 205.
Dakin, W. A.: Canad. Med. Assoc. J., 42: 531–533, 1940.
Hepler, A. B.: Surg., Gynec. & Obst., 53: 688, 1930.
——: J. Urol., 44: 206, 1940.
Hildebrant: Arch. klin. Chir., 48: 343, 1894.
Hinman, F. and Morison, D. M.: J. Urol., 11: 131, 1924.
Kampmeier, V. F.: Surg., Gynec. & Obst., 36: 208–216, 1923.
Lynch, K. D. and Thompson, R. F.: J. Urol., 38: 58–60, 1937.
Meland, E. L. and Braasch, W. F.: J. Urol., 20: 505–519, 1933.
Patterson: Beitr. z. allg. Path., 33: 606, 1903.
Schwartz, J.: J. Urol., 35: 259–263, 1936.
Sinkoe, S. J.: J. Med. Assoc. Ga., 34: 171–178, 1945.
Toulson, W. H. and Wagner, J. H.: Bull. School of Med. Univ. Md., 25–26: 177–184, 1940–42.
Virchow, R.: Ges. Abhandl. z. Wissensch. Med., 1856, p. 864.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

BRANCHED RENAL CALCULI[1]

JAMES T. PRIESTLEY
Division of Surgery, Mayo Clinic

AND

J. HARTWELL DUNN
Fellow in Urology, Mayo Foundation, Rochester, Minnesota

Some years ago we became impressed by the fact that most urologists seemed to have a rather passive attitude toward treatment of the patient who had a branched type of calculus in one or both kidneys. The majority opinion appeared to favor so-called conservative treatment, which in effect amounted to letting nature take its course. A minority opinion favored a more active approach to the problem, with the thought expressed that stones of this type should be treated essentially in the same manner as other types of calculi. Little evidence was found in the literature to support either point of view. Except for the report of individual cases, the English literature on management of branched renal calculi is rather meager. During the past fifteen years, however, Prather, Bugbee, Pollock, Swan and a few others have made contributions to this subject.

The present study was undertaken with the purpose of evaluating clinical experience in the treatment of patients in whom a branched type of renal calculus was present in one or both kidneys. A group of 382 patients seen at the Mayo Clinic in the years 1927 through 1940 have been reviewed. No patient seen since 1940 was included in this study, so that at the time when the study was started a minimal follow-up period of 5 years or more was possible on all patients. Many of these patients have returned repeatedly for observation or treatment and the condition of the remainder was ascertained by a questionnaire letter. For evaluation of late results it was found necessary to divide the entire group of patients into three categories; namely, 1) those who had a branched stone in one kidney, 2) those who had a branched stone in one kidney and an unbranched type of stone in the other kidney, and 3) those who had branched stones in both kidneys. These three groups are considered individually in the discussion of treatment and results.

CLINICAL FEATURES

Sex. In the entire group of 382 patients it was noted that 61 per cent were men and 39 per cent were women, a ratio which is approximately the same as that reported for other types of renal calculi. Although approximately one-half of the men had a unilateral calculus and the other half had bilateral calculi, it was found that 70 per cent of the women had a unilateral stone and only 30 per cent had bilateral stones, a difference between men and women that seems more than incidental; no satisfactory explanation for this difference has been forthcoming.

---

[1] Read at annual meeting, American Association of Genito-Urinary Surgeons, Skytop, Pa., May 14, 1948.

Type of calculous disease. Of the entire group of 382 patients, 234 had a branched stone in only 1 kidney, 80 had a branched stone in 1 kidney and one or more unbranched stones in the other kidney, and 68 had a branched stone in both kidneys. It should be mentioned that in the patients in whom bilateral stones were present the stones did not occur simultaneously in every case although usually they did. It will be noted, therefore, that a total of 148 patients, or 38.7 per cent of the entire group of 382, had bilateral stones, an incidence which is definitely higher than that usually encountered in patients who have unbranched stones, which is approximately 15 per cent. Although the exact significance of this increased tendency to bilateral stones in patients with branched calculi may be somewhat obscure, it does seem apparent that the presence of a branched type of calculus implies a more serious type of disease than that encountered in the average patient with renal calculi.

Symptoms. By far the most common finding in patients with branched renal stones was pyuria, as this was present in 96 per cent of the 382 patients. Although the amount of pyuria varied somewhat during the course of the disease, an estimate revealed that an average of 23 per cent of the patients had what was classified as a grade 1 or 2 pyuria and the remaining 77 per cent evidenced pyuria, grade 3 or 4. Cultures of the urine revealed a wide variety of organisms, with those that split urea being predominant. The fact that virtually all stones of this type are associated with infection is well appreciated.

Of the subjective symptoms, pain was of course the most common, as 68 per cent of the 382 patients complained of pain of some type. In 37 per cent only dull pain was present, in 22 per cent definite attacks of renal colic occurred and in 9 per cent dull pain and severe attacks of colic occurred. It is of interest that in 32 per cent of cases there was no pain. The absence or presence of pain and, if present, its type are of some clinical significance. The patient who had no pain or perhaps only slight intermittent dull pain was likely to present himself for examination only after far-advanced disease existed, unless the stones happened to be detected more or less accidentally. In contrast, severe pain, frequently associated with obstruction to the kidney, commonly brought the patient to his physician promptly. It should be kept in mind that extensive degrees of renal destruction can occur in the absence of any pain. The obvious clinical corollary of this fact is that pain is not a reliable criterion on which to base an opinion regarding the necessity of operation, although it looms large in the mind of the patient as an indication for surgical treatment. Conversely, the patient is inclined to consider the absence of pain as a reason why operation is unnecessary. From the viewpoint of pathologic physiology the folly of this type of reasoning should be appreciated.

Other salient features elicited in the history of the patient who has branched renal stones are hematuria, which occurred in 21 per cent of the 382 cases, and the spontaneous passage of small calculi, which was noted in 22 per cent. Gastro-intestinal symptoms comprised the sole complaint in 3 per cent of all patients. As evidenced by this fact, it is well to remember that occasionally the *patient who has renal calculi may have* symptoms which appear to be entirely unrelated to the urinary tract. In 11 per cent of all patients there were no significant symptoms, the stones being discovered on a routine examination or because of some other extraneous reason which led to a clinical investigation. It is entirely possible that closer questioning of the patients in this category might have elicited a few symptoms of some type but for practical purposes these patients had no significant complaints.

TREATMENT

Treatment of the patient who has a branched renal calculus presents a difficult problem especially if stones of this type are present in both kidneys. Oftentimes, if there are no compelling symptoms present, the patient may not appreciate the threat that exists to renal function, and even his physician may permit the most opportune time for surgical treatment to pass while employing "conservative" treatment. The fallacy of this management is readily apparent when it is realized that progressive renal damage always occurs when a branched type of calculus is present. Sometimes this is a gradual, long drawn out process but other times it is more rapid. The term "silent renal stone" is an unfortunate designation as it implies that such a calculus is a dormant entity of little significance. Obviously the most important consideration in the management of the patient who has a branched type of stone is the preservation of renal function. A greater opportunity to preserve renal function exists early, rather than late, in the course of the disease.

If a branched stone is present in only 1 kidney and the opposite kidney appears to be normal, the problem is not so difficult. Here, as in other surgical lesions of the kidney, however, conservation of renal tissue should be of prime concern. This is particularly true in view of the fact that bilateral occurrence of calculi is definitely more frequent if a branched stone is present than if a simple unbranched type of calculus exists. The development of a stone in the opposite kidney may be slow and may not take place for several years or more but this is no reason for disregarding such a possibility in reaching a decision regarding treatment for the initial calculus. If bilateral stones are present the possibilities of treatment vary considerably and include nonoperative therapy, unilateral nephrectomy, unilateral conservative operation, unilateral nephrectomy and unilateral conservative operation, or bilateral conservative operation. Obviously, if stones are present in both kidneys, conservatism is even more important than if a unilateral calculus exists.

The type of treatment employed in the entire group of 382 patients is shown in table 1. Thus it is seen that in the entire group, surgical treatment was employed in 70 per cent and nonsurgical treatment in only 30 per cent of cases. Many patients included in the latter category were those with extremely advanced and permanent renal damage in whom there seemed to be little opportunity for improvement by operation. Also included in this group were some with serious disease elsewhere in the body which rendered any major surgical procedure too hazardous in comparison with the possible benefits that might accrue from this form of treatment.

The types of operation performed in the 369 cases in which surgical treatment was employed are shown in table 2. It is at once apparent, as one would expect, that conservative surgical procedures were used much more frequently if bilateral stones were present than if only a unilateral calculus existed. Thus, taking the two extremes, nephrectomy alone was performed in 61 per cent of patients who had a unilateral branched stone whereas a bilateral conservative operation was carried out in 50 per cent of patients treated surgically who had branched stones in both kidneys. In deciding for or against a conservative operation for the patient who has a single branched calculus, one must of course remember, when dealing with a patient of advanced years or one in poor general condition, that nephrectomy is a procedure with less immediate risk and more certain to be followed by a smooth postoperative convalescence than is nephrolithotomy.

TABLE 1 *Branched renal calculi· type of treatment*

TYPE OF CALCULI	PATIENTS	TYPE OF TREATMENT, PER CENT	
		Surgical	Nonsurgical
Branched stone one side	234	69	31
Branched stone one side, unbranched stone other side	80	80	20
Bilateral branched stones	68	65	35
Total	382	70	30

TABLE 2 *Branched renal calculi· surgical cases by type of treatment*

TYPE OF CALCULI	PATIENTS	TYPE OF TREATMENT, PER CENT			
		Nephrectomy alone	Unilateral conservative operation	Nephrectomy and unilateral conservative operation	Bilateral conservative operation
Branched stone one side	161	61	39		
Branched stone one side, unbranched stone other side	64	16	17	37	30
Bilateral branched stones	44	11	28	11	50

Hospital mortality which followed the various types of operations is indicated in table 3. As many of the patients who had bilateral calculous disease had each kidney operated on at different times, there are more operations shown in the table than patients. The operative mortality rate of 2.5 per cent for patients with unilateral branched calculus may appear unduly high when compared with the mortality attendant on surgical treatment of patients who had bilateral stones. It must be kept in mind, however, that many patients in the former group had a solitary kidney with perhaps a repeatedly recurring calculus and advanced renal damage. It would seem apparent that surgical treatment of branched renal calculi is not associated with a prohibitive operative risk, especially if the prognosis associated with nonoperative treatment is kept in mind. The mortality rates shown in table 3 should be lower at the present time as many patients included in this table were operated on prior to the advent of chemotherapy and the antibiotics.

TABLE 3. *Branched renal calculi: surgical cases according to hospital mortality*

TYPE OF CALCULI	PATIENTS*	HOSPITAL DEATHS		OPERATIONS†	HOSPITAL DEATHS	
		Number	Per cent		Number	Per cent
Branched stone one side	161	4	2.5	161	4	2.5
Branched stone one side, unbranched stone other side	64	1	1.6	108	1	0.9
Bilateral branched stones	44	3	6.8	71	3	4.2
Total	269	8	3.0	340	8	2.4

* This table is based, in part, on 269 patients. Some patients had more than one operation.

† This table is based, in part, on 340 operations performed on 269 patients.

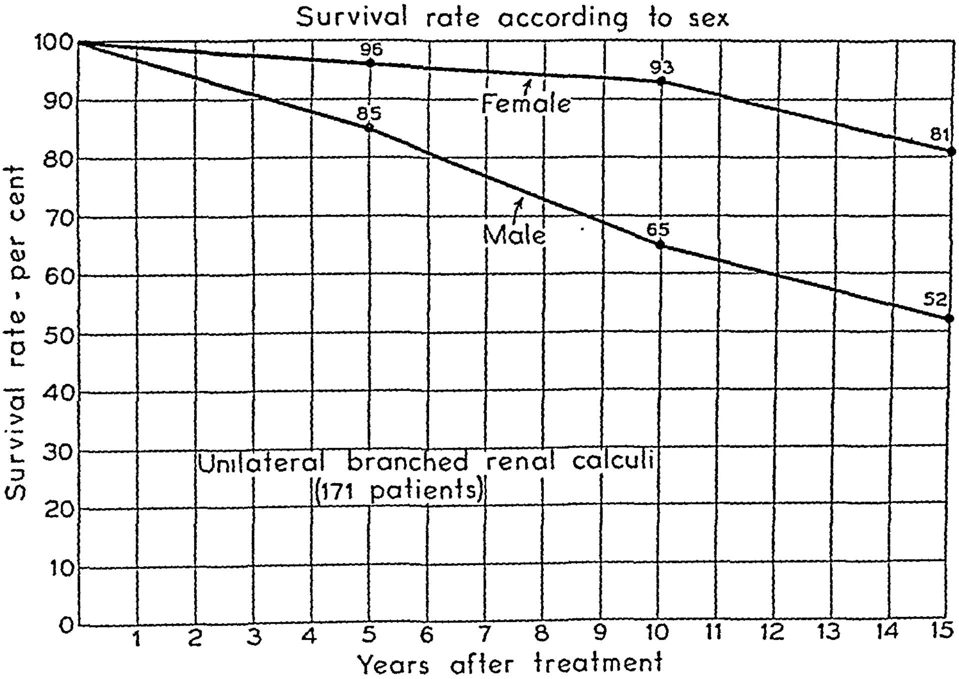


FIG. 1. Survival rate for patients who have unilateral branched renal calculi, according to sex.

LATE RESULTS

In an effort to determine the various factors which influence late results in the treatment of branched calculi, survival rates for these patients were determined according to numerous different factors. Only those which seemed to have clinical significance will be discussed.

Sex. For reasons which are not completely apparent, it was observed that in general the ultimate prognosis for the patient who has a branched calculus, regardless of the type of treatment employed, was more favorable for women than for men (fig. 1). Lower mortality and mortality rates for women as compared with those for men have of course been noted in many other conditions. In regard to all cases of branched renal calculi, whether unilateral or bilateral and whether treated by nonoperative or surgical methods, there is a consistent difference in the late results obtained in men and women, the latter having the *more favorable prognosis.*

Unilateral and bilateral stones. Except in the case of a branched stone in a solitary kidney, bilateral calculous disease usually involved a greater risk for the patient's longevity than a unilateral stone. Thus, in figure 2, it is readily apparent that the patient who has a unilateral branched stone has a greater chance of survival than the patient who has bilateral stones. It is apparent also that the patient who has a branched stone on one side and an unbranched stone on the other side has a better prognosis than the patient who has a branched stone in each kidney. Obviously, a branched type of calculus, which perhaps fills the pelvis and most of the calyces, presents a more serious form of disease than does a single unbranched type of stone.

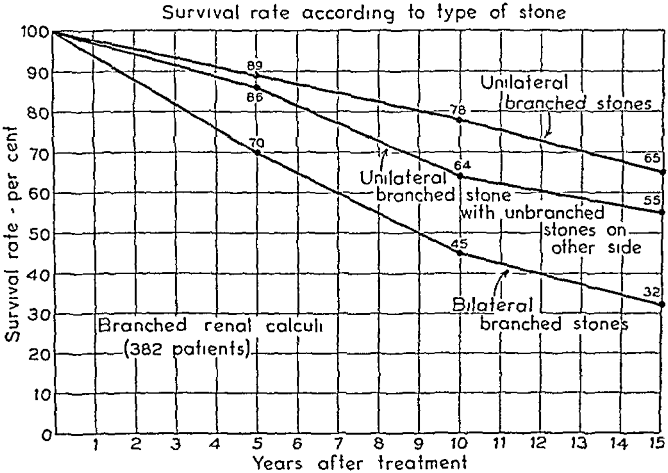


FIG. 2. Survival rate for patients with branched renal calculi, according to unilateral or bilateral existence of stones.

Type of treatment. Survival rates vary significantly according to the type of treatment that is employed. In considering first the patient who has a unilateral branched stone, it is apparent from figure 3, that the best prognosis is afforded the patient who has a conservative operation performed. In contrast, the poorest prognosis exists when nonoperative treatment is employed. Nephrectomy is followed by results which lie between those obtained by the two former methods of treatment. It is probably correct to mention that at least some of the patients in the nonoperative group were those who had a stone in a solitary kidney which was considered to be too extensively damaged to permit a conservative operation. It should be realized that there is necessarily a certain selection of patients in each category of treatment so that the type of treatment given cannot in itself be considered the sole determining factor in the late result obtained. In some cases in which nonoperative treatment was employed, for example, the patient's condition was such that surgical treatment seemed out of the question.

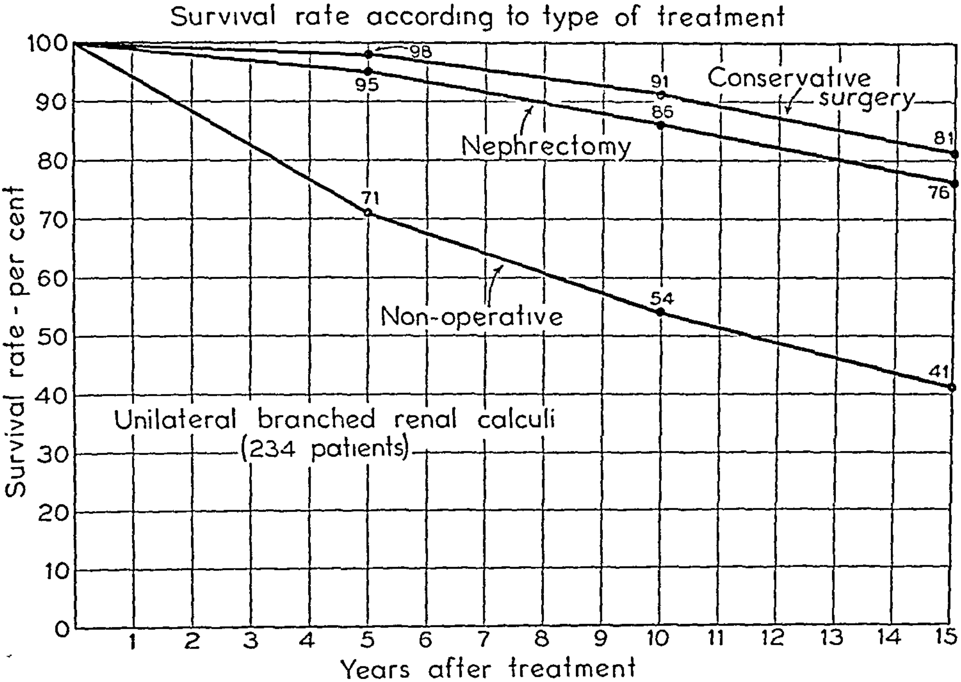


FIG. 3. Survival rate for patients with branched renal calculi, according to type of treatment.

In the group of 144 patients in whom bilateral stones were present, at least one of which was branched in type, it is again apparent that the best results were obtained (fig. 4) in those patients in whom it was possible to do a bilateral conservative operation. Perhaps all the differentiation in results shown in the graph (fig. 4) may not be too significant, but it does seem quite definite, for example, that removal of the stones from both kidneys affords a better outlook than that afforded by nonoperative treatment.

The group of patients in whom bilateral branched renal calculi were present is too small to permit consideration of results obtained with various types of treatment longer than 5 years after operation. It is at once apparent (table 4) that the most favorable survival rates were obtained if removal of the stones from each kidney was accomplished. In contrast, the poorest results followed nonoperative treatment. These facts seem to substantiate our belief that when feasible the most desirable treatment for the patient who has bilateral branched renal calculi is surgical removal of the stones. Palliative measures most often result only in progressive renal damage.

Miscellaneous factors. In addition to the factors mentioned, certain others appear to influence prognosis for the patient who has branched renal calculi.

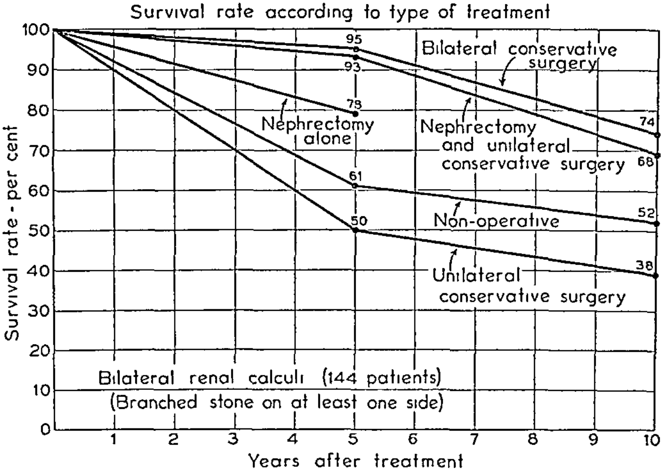


FIG 4 Survival rate for patients with bilateral renal calculi with a branched stone on at least one side, according to type of treatment.

TABLE 4 *Bilateral branched renal calculi: survival rates according to type of treatment*

TYPE OF TREATMENT	PATIENTS TRACED		
	Total	Lived beyond five years	
		Number	Per cent
Nonoperative	20	10	50
Other surgical procedures	22	15	68
Bilateral conservative operation	21	19	95
Total -	63	44	70

Among these may be mentioned the amount of renal damage that exists at the time when treatment is instituted. Obviously, the patient who has had long-standing and progressive renal injury has a less favorable outlook for a good result than the patient who has had a relatively minor degree of damage to the renal parenchyma. In this regard the condition may be likened to that associated with a malignant lesion, as in general the earlier in the course of the disease that the diagnosis is established and treatment instituted the better is the prognosis.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

THE TREATMENT OF URETERAL COLIC AND URETERAL CALCULUS BY THORACOLUMBAR SYMPATHETIC BLOCK: PRELIMINARY REPORT[1]

JOHN T. MACLEAN AND (BY INVITATION) J. J. CARROLL[2] AND H. B. GRAVES[2]

From the Departments of Urology and Anaesthesia, Queen Mary Veterans' Hospital, Montreal, Canada

In 1931 Wharton and Hughson reported 2 cases of intractable ureteral colic relieved by severing the sympathetic nerve supply. In 1934 Hepburn reported 3 similar results. In 1934 Keyser published a paper on the mechanism and clinical management of pain syndromes in the upper urinary tract. In this paper he refers to 2 cases of ureteral colic which were treated by the injection of alcohol into the paravertebral sympathetic ganglia. In 1938 White reported a case in which spasm of the upper ureter was relieved for 1 hour by a sympathetic block of thoracic 12, lumbar 1 and 2. Permanent relief was obtained by dissection of all the nerves surrounding the renal vessels and upper 3 cm. of the ureter. Trimble and Sanford in 1946 reported 1 case of bilateral renal colic and anuria following sulfadiazine therapy, relieved by lumbar sympathetic nerve block. They also report 1 case of ureteral calculus in which the colic was relieved by sympathetic block, and the stone passed spontaneously.

Our interest in this subject arose when we were faced with the problem of providing relief of pain in a patient suffering from severe right sided ureteral colic, when he had already been greatly depressed by previous large doses of morphine. A plain roentgenogram and intravenous pyelograms showed a calculus in the right midureter and a hydronephrosis on the right side.

Consideration of the various morphine substitutes which might be used did not appear to offer much hope. Since the afferent impulses from the ureter pass through the 11th and 12th thoracic, and 1st and 2nd lumbar sympathetic rami, it was decided to see what effect thoracolumbar sympathetic block would have upon the colic.

Accordingly the sympathetic chain on the right side was blocked by the local injection of 2% procaine at the levels thoracic 11 and 12, and lumbar 1 and 2. Relief of pain occurred within 2 minutes and the patient fell deeply asleep. Twelve hours later the colic returned but with decreased severity. The sympathetic block was repeated and the patient obtained almost immediate relief of the pain. The following day the patient had no pain. A plain roentgenogram revealed that the calculus had passed into the bladder. He subsequently voided the calculus without any difficulty.

Being rather surprised and encouraged with this initial success, it was decided that subsequent cases of ureteral colic, in which the diagnosis of calculus had been confirmed and where the calculus was considered to be sufficiently small to pass, would be treated in a similar fashion.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

[2] Now of the Department of Anaesthesia of the Vancouver General Hospital, Vancouver, B.C.

feasible the most desirable treatment for the patient who has bilateral branched renal calculi is surgical removal of the stones. Palliative measures most often result only in progressive renal damage.

Miscellaneous factors. In addition to the factors mentioned, certain others appear to influence prognosis for the patient who has branched renal calculi.

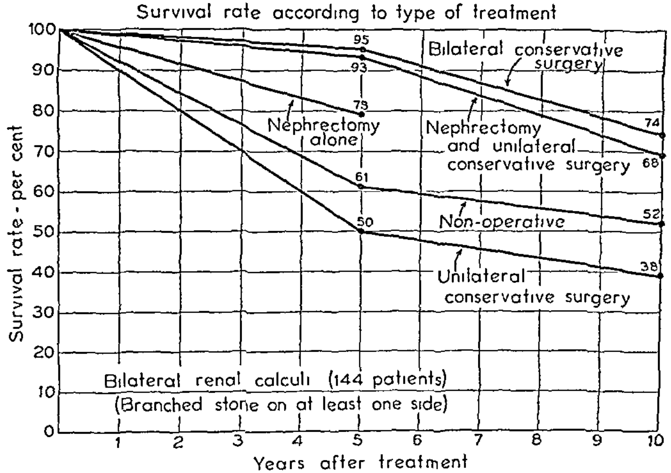


FIG. 4. Survival rate for patients with bilateral renal calculi with a branched stone on at least one side, according to type of treatment.

TABLE 4. *Bilateral branched renal calculi: survival rates according to type of treatment*

TYPE OF TREATMENT	PATIENTS TRACED		
	Total	Lived beyond five years	
		Number	Per cent
Nonoperative	20	10	50
Other surgical procedures	22	15	68
Bilateral conservative operation	21	19	95
Total -	63	44	70

Among these may be mentioned the amount of renal damage that exists at the time when treatment is instituted. Obviously, the patient who has had longstanding and progressive renal injury has a less favorable outlook for a good result than the patient who has had a relatively minor degree of damage to the renal parenchyma. In this regard the condition may be likened to that associated with a malignant lesion, as in general the earlier in the course of the disease that the diagnosis is established and treatment instituted the better is the prognosis.

Late results vary somewhat, depending on the type and amount of pain that has been present. Thus, the patient who has experienced dull pain has the best prognosis, the patient who has colicky pain, the next best prognosis, and the patient who has had no pain, the poorest outlook. Although the actual reasons for these variations are not definite, it seems likely that they may be explained in the following manner. The patient who has no pain probably does not consult a physician until the calculous disease has been present a long time and perhaps in some cases not until symptoms of renal insufficiency supervene. Under these circumstances, an advanced degree of renal damage already has occurred at the time when treatment is undertaken. In contrast, the patient who has dull pain seeks medical attention earlier. As mentioned, the prognosis for the patient who has a collicky type of pain lies between that for the one who has no pain and the one who experiences full pain. Perhaps this is true because although the patient who has a colicky type of pain may seek medical attention early, the occurrence of colicky pain may indicate an acute obstruction which in itself is associated with some hazard and in addition causes a certain amount of renal damage.

The extent of pyuria may have some bearing on the ultimate prognosis although this is not too definite nor too easy to determine. The extent of pyuria manifested by a patient with branched calculi may vary considerably from time to time which makes classification of patients according to extent of pyuria difficult. In general, those with extensive infection have a somewhat less favorable prognosis than those who have only a minimal amount of infection.

Comment. Unfortunately, the recurrence rate of stone is high following removal of a branched renal calculus. In fact, one can even say that recurrence is the rule, rather than the exception. Despite this fact it is apparent from the present study that the ultimate prognosis is more favorable if the original stones are removed than if they are not removed. In some patients subsequent operation for recurrent stones may be necessary. In others, only small recurrent calculi may form and either they may pass spontaneously or remain for some time without growing and without causing significant renal damage. Elimination of infection and establishment of good drainage from all parts of the kidney, if possible, are important in prevention of recurrence. In our experience, hyperparathyroidism is seldom associated with a branched type of renal calculus. As a general rule it is not our practice to treat recurrences surgically until it is evident that they are causing renal damage unless treatment must be instituted because of the severity of symptoms, which is unusual. By far the majority of branched calculi are composed of calcium phosphate and carbonate, but occasionally a cystine, uric acid or other type of calculus may be encountered. Chemical analysis should always be performed on the calculus removed because of any possible information it might give in directing treatment to prevent recurrence. Our experience with the use of various solvent solutions has not been too satisfactory.

It should be kept in mind that most patients with bilateral branched renal calculi already have serious reduction in renal function at the time when surgical treatment is first undertaken. This may not be manifested by the ordinary tests of renal function and becomes evident only when some additional load is placed on the kidneys, such as that associated with a surgical operation. The renal reserve is seriously depleted in these patients and a full-blown renal insufficiency may become apparent during the early postoperative period. This manifestation is of course augmented by the immediate reduction of renal function which results from trauma to the kidney at the time of operation. One must detect postoperative renal decompensation at once and institute appropriate supportive therapy if operative mortality is to be kept at a minimum.

The fact that a patient has gross renal inadequacy at the time when he is first seen does not necessarily mean that surgical treatment is out of the question. An effort should be made to determine the basis of the insufficiency whether it is dependent to a considerable extent on obstruction or to irreparable and irreversible damage to the renal parenchyma. In the latter case, surgical treatment offers little; however, in the former case operation may be followed by a most gratifying result. Usually, as in most clinical conditions, a mixed picture exists and the surgeon must exert careful clinical judgment in reaching the decision for or against surgical treatment.

SUMMARY

A group of 382 patients seen in the years 1927 through 1940, all of whom had a branched calculus in one or both kidneys, has been reviewed. Certain clinical aspects of these patients are discussed but most consideration is given to the treatment and late results that have been obtained.

From this study it would appear that a branched renal calculus can be removed by nephrolithotomy with a reasonable operative risk. The results of surgical treatment are superior to those which follow nonoperative management. In general, the best results are obtained from conservative surgical treatment in which the stone or stones are removed but nephrectomy is not performed. Other factors which influence results are mentioned.

REFERENCES

Allen, E. V.: The relationship of sex to disease. Proc. Staff Meet., Mayo Clin., 8: 213–216, 1933.
Bugbee, H.: Nephrolithotomy for recurrent branching calculi. Tr. Am. A. Genito-Urin. Surg., 37: 123–134, 1944.
Pollock, L. H.: Staghorn calculus removal by V-shaped nephrotomy. J. Missouri M. A., 39: 48–50, 1942.
Prather, G. C.: A method of hemostasis during nephrotomy for large kidney calculi. J. Urol., 32: 578–599, 1934.
Prather, G. C.: Review of the "V" type nephrotomy for staghorn calculus with special reference to final results. Am. J. Surg., 39: 589–601, 1938.
Priestley, J. T.: Treatment for unilateral and bilateral, staghorn renal calculi. J. Urol., 42: 933–942, 1939.
Priestley, J. T. and Braasch, W. F.: Late results in the conservative management of nephrolithiasis. J. A. M. A., 109: 1703–1705, 1937.
Rubin, J. S.: Giant renal calculus in bilateral nephrolithiasis. Tr. West S. A., 12: 88–89, 1944.
Swan, R. H. J.: Massive bilateral renal calculi. Proc. Roy. Soc. Med., 26: 487–488, 1933.
Walters, W., Counseller, V. S. and Priestley, J. T.: The treatment of unilateral and bilateral "stag-horn" renal calculi. Proc. Staff Meet., Mayo Clin. 9: 144–147, 1934.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

THE TREATMENT OF URETERAL COLIC AND URETERAL CALCULUS BY THORACOLUMBAR SYMPATHETIC BLOCK: PRELIMINARY REPORT[1]

JOHN T. MACLEAN AND (BY INVITATION) J. J. CARROLL[2] AND H. B. GRAVES[2]

From the Departments of Urology and Anaesthesia, Queen Mary Veterans' Hospital, Montreal, Canada

In 1931 Wharton and Hughson reported 2 cases of intractable ureteral colic relieved by severing the sympathetic nerve supply. In 1934 Hepburn reported 3 similar results. In 1934 Keyser published a paper on the mechanism and clinical management of pain syndromes in the upper urinary tract. In this paper he refers to 2 cases of ureteral colic which were treated by the injection of alcohol into the paravertebral sympathetic ganglia. In 1938 White reported a case in which spasm of the upper ureter was relieved for 1 hour by a sympathetic block of thoracic 12, lumbar 1 and 2. Permanent relief was obtained by dissection of all the nerves surrounding the renal vessels and upper 3 cm. of the ureter. Trimble and Sanford in 1946 reported 1 case of bilateral renal colic and anuria following sulfadiazine therapy, relieved by lumbar sympathetic nerve block. They also report 1 case of ureteral calculus in which the colic was relieved by sympathetic block, and the stone passed spontaneously.

Our interest in this subject arose when we were faced with the problem of providing relief of pain in a patient suffering from severe right sided ureteral colic, when he had already been greatly depressed by previous large doses of morphine. A plain roentgenogram and intravenous pyelograms showed a calculus in the right midureter and a hydronephrosis on the right side.

Consideration of the various morphine substitutes which might be used did not appear to offer much hope. Since the afferent impulses from the ureter pass through the 11th and 12th thoracic, and 1st and 2nd lumbar sympathetic rami, it was decided to see what effect thoracolumbar sympathetic block would have upon the colic.

Accordingly the sympathetic chain on the right side was blocked by the local injection of 2% procaine at the levels thoracic 11 and 12, and lumbar 1 and 2. Relief of pain occurred within 2 minutes and the patient fell deeply asleep. Twelve hours later the colic returned but with decreased severity. The sympathetic block was repeated and the patient obtained almost immediate relief of the pain. The following day the patient had no pain. A plain roentgenogram revealed that the calculus had passed into the bladder. He subsequently voided the calculus without any difficulty.

Being rather surprised and encouraged with this initial success, it was decided that subsequent cases of ureteral colic, in which the diagnosis of calculus had been confirmed and where the calculus was considered to be sufficiently small to pass, would be treated in a similar fashion.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

[2] Now of the Department of Anaesthesia of the Vancouver General Hospital, Vancouver, B.C.

In order to evaluate this method of treatment, it is considered to be of more value to report all the cases that have come under the care of the authors rather than only those treated in the Military Hospital. Fifteen cases are presented.

TECHNIQUE OF THORACOLUMBAR SYMPATHETIC BLOCK FOR URETERAL COLIC

The technique for blocking the sympathetic chain is that described by Labat with a few modifications of our own

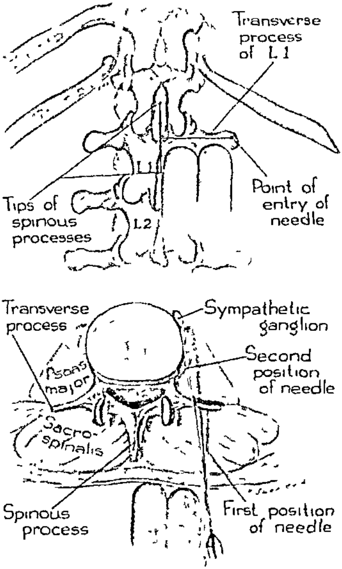


FIG 1 Showing landmarks and technique of injection into lumbar sympathetic chain Ten cubic centimeters of 2 per cent procaine is injected at each selected level (Th 11, 12, and L 1).

The patient is placed in a prone position and pillows placed under the abdomen to flex the back. The spinous processes of D.12 L.1 and 2 are found. Skin wheals are raised on the affected side, 4 cm. lateral to the processes (4 cm. is approximately the breadth of two fingers in the average male). A No. 22, 10 cm. needle (15 cm. in stout patients) with a movable rubber marker is inserted through the skin wheal to strike the transverse processes. The rubber marker is then set on the needle 5 cm. above the skin. The needle is withdrawn very slightly, slipped above the transverse process and reinserted until the marker reaches the skin. The needle point is now 5 cm. anterior to the transverse process and very close to the sympathetic chain. Five to 10 cc of 2 per cent procaine is then injected through each needle at the above mentioned levels. (See figure 1.)

The procedure is easily done and after a little experience is practically painless to the patient. If the block is successful, there will be *complete relief of* colic within a few minutes.

We have measured a large number of lumbar vertebrae, and have found that in all adults the distance from the posterior surface of the transverse process to the anterolateral surface of the body, where the sympathetic chain lies, is always very close to 5 cm. Therefore, we no longer follow Labat's technique of sliding the needle along the side of the body until the needle is felt to have reached the anterior surface. This was a painful and rather inaccurate method.

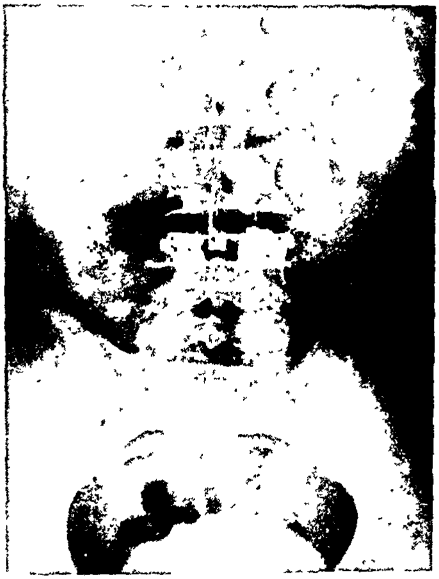


FIG. 2. Case 2. Showing obstruction of right ureter by calculus at pelvic brim with dilatation above. Colic was completely relieved by sympathetic blocks but position of calculus was unaltered. Ureterolithotomy was required.

RESULTS OF TREATMENT

It will be seen from tables 1 and 2 that of the 15 patients treated, 13 *had colic at the time of administering* the sympathetic block. All 13 cases obtained complete relief of the colicky pain within a few minutes after the local injection of 2 per cent procaine into the thoracolumbar sympathetic chain on the affected side.

Lapides states that "tonus and rhythmic contraction of the intact human ureter are entirely independant of the central nervous system including the autonomic nervous system and all its ganglia". He states that ureteral peristalsis remains vigorous despite the inactivation of its total nerve supply by procaine spinal anesthetic. Our findings do not conflict with those of Lapides, but do indicate that sympathetic block provides complete relief of pain in cases suffering from ureteral colic.

In 15 cases treated, the calculus passed spontaneously in 8 (53.3 per cent) without further treatment. One was retrieved with the stone basket. It might be reasoned that the calculi would have passed spontaneously without the sympathetic block. This may be true, but it is a fact that in 4 of the 8 cases (50 per cent) in which the calculus did pass spontaneously, previous instrumentation had failed to retrieve the calculus. We are not in a position to say whether peristalsis in the ureter was altered, although it was our impression, clinically, that the sympathetic block hastened and facilitated the passage of the calculi in some cases. This would imply that the calculus was small enough to pass, and was not embedded in mucous membrane.

TABLE 1

CASE NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Age	32	28	30	27	27	20	26	54	32						
Roentgenogram	?	+	+	+	?	+	+	+	+	+	+	+	+	+	+
Side															
Right	M ⅓	L ⅓	L ⅓	L ⅓	L ⅓			U ⅓		L ⅓		L ⅓			
Left						L ⅓	L ⅓		M ⅓		M ⅓		M ⅓	M ⅓	M ⅓
Previous instrumental attempts			1				3	1		2	1				
Pain relieved by block	+	+	+	+	+	0	+	0	+	+	+	+	+	+	+
Passed calculus	+			+	+		+			+	B	+	+	+	$\boxed{L}$
Ureterolithotomy		+	+			+		+	+						

Note:
M—Middle
L—Lower
U—Upper
B—Basket
$\boxed{L}$—Unaltered
0—None.

TABLE 2

	NUMBER OF CASES	PER CENT
Site of calculus		
Upper ⅓	1	6.5
Middle ⅓	6	40
Lower ⅓	8	33.3
Complete relief of pain with block (13 cases)	13	100
End result		
Passed calculus spontaneously	8	53.3
Instrumental removal	1	6.5
Ureterolithotomy	5	33.3
Unchanged	1	6.5

was brought to the operating room for cystoscopic examination and retrograde pyelograms. It was found that the right ureteral obstruction had been completely relieved, the patient evidently had passed the calculus during the night. There has been no recurrence of symptoms.

Case 6. Diagnosis: Left ureterolithiasis. G. W., aged 20 years, was admitted to the Queen Mary Veterans' Hospital on January 10, 1947 with the following history. In the first week of December 1946, he had noticed that his urine was red on two ocasions, but there were no clots, and he blamed the discoloration on some medicine he had taken for a cold. On January 2, 1947, he felt a very sharp, colicky pain in his left lower quadrant. The pain radiated down to his genitalia and up behind his ribs. The pain lasted 1 hour. Similar attacks occurred on January 4 and 9, lasting about 4 hours. He had another recurrence on January 10, the pain lasting the whole day and he was admitted to the hospital.

A roentgenogram revealed 2 small calculi in the lower pole of the right kidney, and a large calculus in the middle third of the left ureter. The urine was positive for blood. An intravenous pyelogram on January 13, 1947, revealed that the two small calculi on the right side were in the lower and minor calyces of the right kidney. There was a large calculus in the left ureter, 2½ inches below the ureteropelvic junction with a dilated ureter proximal to the calculus.

A left thoracolumbar sympathetic block with 2 per cent procaine was done at sites T 11, 12 and L 1 and 2 on January 13, 1947 with complete relief of pain, but no alteration in the position of the calculus. Left ureterolithotomy was done on January 15, 1947. Convalescence was uneventful and the patient was discharged from hospital on February 17, 1947.

Comment: Sympathetic block on this patient did not alter the position of the stone. It was felt that the stone was too large to pass spontaneously and had become impacted.

Case 7. Diagnosis: Left ureterolithiasis. J. L. B., aged 26 years, had been admitted to the hospital on January 22, 1947, complaining of colicky pain in the left loin of 5 days' duration. The history dated back to June 1945, since which time he had had recurrent attacks of colicky pain in the left loin. He had been in the Queen Mary Veterans' Hospital in October and November 1946, where a diagnosis of left renal calculus in the left superior calyx had been made.

A roentgenogram on admission in January 1947 showed the calculus to be situated at the mid-ureter (fig. 3, *A*). On January 31, the ureter below the calculus was dilated and an attempt made to remove the stone instrumentally. On February 4, 1947, he felt a dull pain in his left loin and had some hematuria. A roentgenogram taken the following day showed the calculus to have passed almost down to the bladder (fig. 3, *B*). Intravenous pyelograms on February 20 showed delayed excretion, up to 1 hour in the left kidney; the calculus still being present in the lower ureter. Following this, he was taken to the cystoscopic room on three different occasions where attempts to dilate the distal end of the ureter and remove the stone were unsuccessful. It was possible to get above this stone for a distance of only 3 cm. On March 13, 1947, a sympathetic block was done on the left side at sites L 1, 2 and 3 with 2 per cent procaine. Four hours after the block the patient voided the stone without any discomfort. Subsequent films showed no calculus in the left kidney, ureter or bladder. He was discharged from hospital on March 18, 1947 as cured and fit to work.

Case 8. Diagnosis: Right ureterolithiasis. A. S., aged 54 years, had suffered from recurrent attacks of colicky pain in his right flank for 6 months. He was admitted to the Queen Mary Veterans' Hospital in April 1947. An intravenous pyelogram series on April 5 revealed a bifid right ureter and a calculus at the junction.

An attempt to remove the calculus by cystoscopy on April 8 was unsuccessful. Thoracolumbar sympathetic blocks on the right side at sites L 1, 2, 3 and 4 with 2 per cent procaine which were done on April 9 and 10, did not affect the position of the calculus. Cystoscopy was repeated on April 21, 1947 and the calculus moved about 2 inches. Another thoracolumbar block was done on April 22, 1947. The position of the calculus remained unchanged.

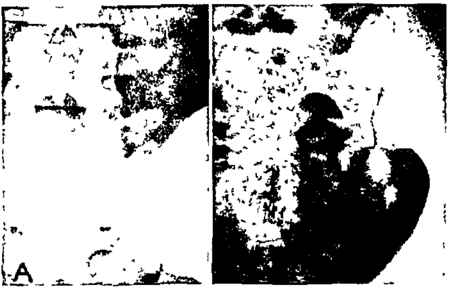


Fig. 3. Case 7. *A*, left, showing position of calculus in left midureter on admission to hospital. *B*, right, five days later, showing calculus in left lower ureter. Repeated attempts to move this instrumentally were unsuccessful. Calculus passed spontaneously 4 hours after thoracolumbar sympathetic block.

Comment: Thoracolumbar sympathetic blocks had no effect on the position of the calculus in this case.

Case 9. Diagnosis: Left ureterolithiasis. J. B., aged 32 years, experienced acute abdominal pain on September 15, 1947. Examination revealed a left ureteral calculus at the midureter, confirmed by a plain roentgenogram and intravenous pyelogram series.

Two left thoracolumbar sympathetic blocks with 2 per cent procaine were done on September 24, 1947. There was complete relief of pain, but the stone failed to move, and it was thought that the stone was impacted. Ureterolithotomy was done on September 25, 1947.

Comment: Thoracolumbar sympathetic blocks relieved the patient's pain, but did not alter the position of the calculus.

Case 10. Diagnosis: Right ureterolithiasis. Mrs. D. was seen in October 1947. A calculus was lodged at the right ureterovesical junction, associated with severe colic and hematuria. Two attempts to remove the calculus instrumentally at cystoscopy had been unsuccessful.

On October 14, 1947 the right sympathetic chain was blocked with 2 per cent procaine at levels D 12, L 1. There was immediate relief of colic and the stone passed spontaneously within the next 24 hours. There has been no recurrence of her complaints.

Case 11. Diagnosis: Left ureterolithiasis. Mr. H. was seen in October 1947, complaining of general malaise for 6 days, acute pain in left flank radiating to the left testicle, and nausea and vomiting for 4 days, frequency and dysuria for 7 days. A roentgenogram showed a calculus in left ureter at level of L 3–4.

The left sympathetic chain was blocked at levels D 12, L 1 and 2, with immediate relief of all complaints. However, the calculus passed only as far as the ureterovesical junction, from where it was instrumentally removed a month later.

Case 12. Diagnosis: Right ureterolithiasis. Mr. H. was admitted to the hospital, complaining of severe colic-like pain in the right costovertebral angle, radiating down to the right groin, thigh and testicle, of 18 hours' duration. A roentgenogram showed a right ureteral calculus about 2 inches from the bladder (fig. 4, *A*).

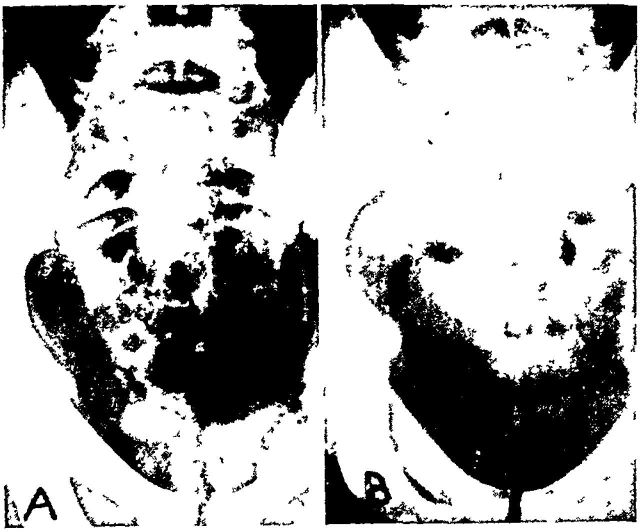


FIG 4. Case 12. *A*, left, showing position of calculus in right lower ureter about 2 inches from bladder. Patient had had colic for 1 week *B*, right, showing absence of calculus 3 days after block of sympathetic chain Calculus was passed spontaneously.

The sypathetic chain was blocked at levels D 12, L 1 and 2, with immediate relief of complaints. The stone was passed 3 days later without discomfort (fig. 4, *B*).

Case 13. Diagnosis: Left ureterolithiasis. Mr. M. was seen in November 1947. He gave a history of ureteral colic of 2 days' duration with roentgenographic evidence of a small calculus in left ureter at level of L 3.

The left sympathetic chain was blocked with 2 per cent procaine at levels D 12 and L 1.

Following the block, there was immediate relief of colic. His urine was collected and strained but the stone was not found. Roentgenograms taken the following day showed no evidence of the calculus and it was assumed that it had passed. In the ensuing 5 months he has had no recurrence of his complaints.

Case 14. Diagnosis: Left ureterolithiasis. Mr. W. was seen in November 1947. He complained of severe colic in the left side of 24 hours' duration. Roentgenograms showed a large calculus in his left midureter, opposite the transverse process of the third lumbar vertebra (fig. 5, *A*).

The left sympathetic chain was blocked with 2 per cent procaine at levels D 12 and L 1.

Within a few minutes there was complete relief of his pain. He was returned to the ward and advised to drink as much fluid as possible. An attempt was made to collect and strain his urine but he was not very cooperative and the stone was not found. However, he had no recurrence of his colic and x-rays taken the following day showed the stone to be absent (fig. 5, *B*). In the ensuing 5 months there has been no recurrence of his complaints.

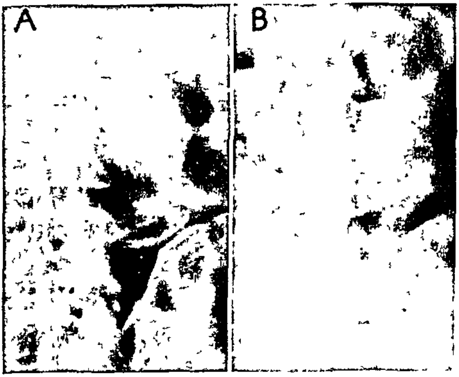


FIG. 5. Case 14 *A*, left, plain roentgenogram on admission, showing calculus opposite transverse process of the 3rd lumbar vertebra on left side. *B*, right, plain roentgenogram taken 24 hours after sympathetic block, showing that calculus has passed.

Case 15. Diagnosis: Left ureterolithiasis. Mr. C. was seen in November 1947. He complained of severe left lower quadrant colic and hematuria. A roentgenogram showed 2 pea-sized calculi in the left ureter at level of L 3 and 2 larger ones in the kidney pelvis. A diagnosis of left ureteral colic and ureterolithiasis was made.

The left sympathetic chain was blocked with 2 per cent procaine at levels T 12 and L 1 and 2. Within a few minutes there was complete relief of pain. He was returned to his ward in Fowler's position and orders were left for forced fluids. Following the sympathetic block this man had no further complaint of colic. However, he did not pass his stones. On cystoscopic examination 1 week later, a ureteral catheter was passed readily to the kidney pelvis without evidence of obstruction. A pyelogram done at this time showed the calculi to be still present in both the ureter and kidney pelvis. He has had no recurrence of his complaints in the ensuing five months.

Comments: The colic in this case was relieved by sympathetic block. The position of the calculi was unchanged.

CONCLUSIONS

A technique for the relief of pain in ureteral colic by thoracolumbar sympathetic block is presented.

In all 13 cases in which colic was present at the time of administering the sympathetic block, the relief of pain was complete and occurred within a few minutes. Of the 15 in which a calculus was present, 8 (53.3 per cent) passed the calculus spontaneously, and 1 was obtained with the stone basket. Of these, 4 (50 per cent) had had previous unsuccessful instrumentation.

In cases of ureteral calculus in which the calculus is considered to be of a sufficiently small size to pass down the ureter, it is thought that sympathetic block as well as giving complete relief of pain, may facilitate passage of the calculus. A sympathetic block does not commit one as to what the future treatment shall be in any given case.

Many of the private patients have been treated on an ambulatory basis. They have the sympathetic block performed at the hospital in the morning, and then go home. They may spend the rest of the day as they wish, being only moderately restrained in their activities.

Medical Arts Bldg., Montreal, Canada.

REFERENCES

De Bakey, M.: Technique of lumbar sympathetic trunk injection. Bull. U. S. Army, M. Dept., No. 73; pp. 23–28, 1944.

Hepburn, T. N.: Denervation and displacement of the ureter for exaggerated renal colic. New Eng. J. Med., **210:** 1255, 1934.

Keyser, L. D.: Pain syndrome in the upper urinary tract. South Med. J., **29:** 953, 1936.

Labat, G.: Regional Anaesthesia: Its Technique and Clinical Application. Philadelphia. W. B. Saunders Co., 1930, 2nd ed., p. 567.

Lapides, J. Physiology of intact human ureter. J. Urol., **59:** 501, 1948.

Mendel, F.: Paravertebral Block. New York: Grune and Stratton, 1947, pp. 83–86.

Trimble, I. R. and Sanford, M. C.: The relief of renal colic and renal suppression; preliminary report. J. Urol., **55:** 4, 1946.

Wharton, L. R. and Hughson, W.: Denervation of the ureter; a new operation for cure of persistent painful ureteral spasm; report of cases. J. Urol., **25:** 145, 1931.

White, J. C. and Smithwick, R. H.: The Autonomic Nervous System. New York: Macmillan Co., 1941, 2nd ed., p. 384.

The Journal of Urology
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DISCUSSION

Dr. Linwood D. Keyser (Roanoke, Va.): Dr. MacLean and his colleagues have presented an excellent contribution to the treatment of ureteral colic and stone. I am particularly interested because I have used a somewhat similar procedure with increasing frequency since 1930, when I began to apply the technique of Labat in treating colic and pain in the upper urinary tract. However, most of my cases were treated for noncalculous pain syndromes, ureterospasm and so-called ureteral stricture. With good blocking of the splanchnic nerves or rather of the ganglia which supply them, we may achieve a remarkable relief of pain. We keep a tray set up for this purpose in our hospital supply room and if a patient comes in with renal or ureteral colic, thoracolumbar block is one of our first considerations.

The method has not been used alone for treatment of ureteral calculi but as an adjuvant to passage of catheters by cystoscopy. After Dr. MacLean's report we shall certainly want to see if many of these ureteral calculi will pass spontaneously with this type of anesthesia and the ureteral relaxation which ensues.

In dilating spastic ureters or passage of catheters beyond calculi in the lower ureter, sympathetic block is of great value. The ureteral orifices frequently lie open and the passage of one or more catheters is usually achieved more easily than with any type of anesthesia previously used.

In cases when we contemplate denervation of the renal pelvis and ureter, preliminary sympathetic block well performed may give an idea of what may be expected from such an operation, if taken with other criteria such as urography and the elimination of orthopedic, gastro-intestinal or other possible pain producing pathological changes. The method is with modifications being widely used by orthopedic, general and neurologic surgeons.

Sympathetic block is not without some hazards, several of which may be mentioned. The dura extends along the nerve roots a variable distance within the intervertebral foramina and can be punctured if one hugs the vertebral body too closely in inserting the needle. Aspiration before injection of the solution should be meticulously observed in order to prevent a massive spinal anesthesia with attendant disaster. Again the injection of 20 to 30 cc of 1 or 2 per cent novocaine at the site of the sympathetic ganglia affords ready absorption in some patients from a wide area. Some of them will develop pallor, weak and rapid pulse, shallow respiration and a drop in blood pressure. Occasionally they may require immediate resuscitation with oxygen, intravenous glucose, and cardiorespiratory stimulants. For this reason we prefer to have the patient in a hospital and do not carry out the procedure in the office. Also we divide the dosage, waiting at least 10 minutes after the injection of the first 10 cc to note the patient's reaction. To date we have had no serious reactions but we have had on several occasions a few anxious moments which make us treat the procedure with respect.

One slide presented shows the innervation of the kidney pelvis and ureter and the relatiou of the aorticorenal and ureteral plexuses to the sympathetic chain.

A second slide shows the posterior splanchnic block of Kappis, as modified by Labat. As it involves the impingement of the needle against the vertebral body and withdrawal and reinsertion until the needle passes this body, it is, as Dr. MacLean has pointed out, a rather painful procedure and one we now rarely use.

Another slide shows the technique of Ochsner and De Bakey, one which we prefer because of less attendant pain and which is similar to that described by our essayists.

On the whole my experience with sympathetic block for renal and ureteric pain has been satisfactory. Pain is almost immediately relieved, the anesthesia lasts for a number of hours and the intensity of the pain is diminished for a longer period. The relaxation and anesthesia of the ureter are remarkable and much better than that achieved with spinal or general anesthesia.

The remarkable number of cases in which calculi have passed without catheter manipulation, as reported by Dr. MacLean, would certainly justify more extensive trial of the procedure he has so well described.

DR. PAUL J. SOLEY (Hempstead, L. I., N. Y.): I want to take only a minute to relate an experience which we had with thoracosympathetic block. We had a patient who had anuria and, after trying many forms of therapy, we called in a neurosurgeon to do a thoracosympathetic block. He was a thoroughly competent man. He placed the needle in the customary way and injected about 16 cc of 2 per cent novocain, and within 3 minutes the patient was dead.

We believe that the reason for this accident was that he injected it into the vein directly. The anatomy there is such that immediately anterior to the lumbar vertebra there is a rich system of veins. It drains the lumbar region having connection with the inferior vena cava and it also drains into the azygous system which is its equivalent in the thorax.

I mention this experience for what it may be worth to those doing thoracosympathetic block. It would seem that the procedure is not without danger.

DR. JOHN T. MACLEAN (Montreal, P. Q.): I wish to thank Dr. Keyser and Dr. Soley for their discussion. I neglected to say that the amount of anesthetic we have been using is usually 5 to 10 cc of 2 per cent procaine at each of the selected levels. So far we have had no bad effects whatsoever, and do not hesitate, once the anesthetic is given, to get the patient up off the table and have him walk, if he so desires. I should have stated that Drs. Carroll and Graves are highly skilled anesthetists and have given all the anesthetics in the cases reported.

THE JOURNAL OF UROLOGY
Vol 61 No 2 February 1949
Printed in U S A

CLINICAL INTERPRETATION OF PYELO-URETERAL DILATATION OF PREGNANCY BASED UPON EXPERIMENTAL STUDIES[1]

RALPH H JENKINS AND G VAN WAGENEN

From the Department of Surgery, Section on Urology, and the Department of Obstetrics and Gynecology, Yale University School of Medicine, and the Grace New Haven Community Hospital, New Haven, Conn

Pyelo ureteral dilatation, which occurs in about 95 per cent of first pregnancies, is considered to be the predisposing cause of pyelitis of pregnancy The early explanation of these changes in the pelvis and ureter was that the cause is mechanical in nature, having to do with the anatomical relationships of the enlarged uterus within the pelvic brim The close proximity of the base of the bladder to the enlarged cervix and uterus was thought to exert pressure on the ureter and to cause an ureteral obstruction For three quarters of a century this explanation was considered an adequate one, and most text books still acquiesce this explanation Other observers have entertained the new concept of hormones as a factor in causing atony of the ureter during pregnancy They feel that simple mechanical obstruction cannot be the whole cause of ureteral dilatation under these circumstances

The writers (1939) have shown that ureteral dilatation occurs in the Rhesus monkey just as in the human This was demonstrated by means of intravenous urograms in the later months of pregnancy Other critical data in the physiology of reproduction in this species are also strikingly similar to those of women, for example, the length of the menstrual cycle in this monkey is 28 days, and the 6 months gestation period (168 days) is longer than in other laboratory animals

Experimentally it has been shown in our laboratory that the fetus can be absent for the greater part of the normal length of gestation without interrupting the physiological state of pregnancy (van Wagenen and Newton) In extension of this work in 1939 we showed that if the fetus alone is removed by abdominal hysterotomy, the placenta remaining functional in the uterus, the urinary tract retained the characteristics of the pregnant condition When the operation is performed in the latter part of pregnancy, after the 'hydro ureter of pregnancy' has been established, the dilatation may be seen to persist and even to progress This occurs in spite of the fact that the weight and size of uterine contents have been diminished far below that which had been attained before obvious dilatation of the ureter has occurred When the fetus is removed in the early half of pregnancy the hydro ureter can arise and be maintained until the placenta is spontaneously expelled at a time compatible with the birth of a viable infant This even further disqualifies the weight and size of the uterus with its contents as the cause of ureteral dilatation

In a recent publication (1948) we reported some results from a study of several hundred pregnancies in the monkey We found three instances in which there was spontaneous death of the fetus while the placenta remained hormonally active. Ureteral dilatation was demonstrated in each of these animals. These cases of spontaneous death of the fetus parallel our earlier experiments, in which the fetus alone was surgically removed during pregnancy. Thus, pyelo-ureteral dilatation of pregnancy is dependent upon the endocrine function of the placenta *maintaining the physiological state of pregnancy, independent of the continued presence or life of the fetus.*

---

[1] Read at annual meeting, American Urological Association, Boston, Mass , May 18, 1948.

Those observers who adhere to the mechanical cause of ureteral dilatation of pregnancy continue to ask many questions which are difficult to answer. We are frequently asked: "Why is the dilatation more frequent and greater in the right ureter than the left?" Our answer is that we do not know, but it is known that in the majority of pregnancies dilatation occurs in both ureters and in some cases only the left ureter is involved. Another favorite query, "How can you expect to have an organ the size of the uterus after the fourth month in the pelvic cavity of a woman without showing some pressure upon the ureters?" Our answer to this question would be that ureteral dilatation is not associated with every pregnancy and it is common not to have dilatation after the second pregnancy. This brings up the question as to whether hormonal treatment is of any value in these cases. In a previous paper (1943) we spoke briefly of some negative results in the experimental use of various hormones. However, Boland (1943) has been able to demonstrate increased tone of the ureter following administration of stilbestrol in a few cases when treatment was started 48 hours after delivery. We are reluctant to recommend hormonal therapy, but the study of this field is still in its infancy and with our present basic knowledge it is hoped that further investigation will lead to the use of helpful therapy.

In 1943 we presented an experimental study of pyelo-ureteral dilatation in successive pregnancies in the monkey. It was found that the greatest dilatation occurred in the first pregnancy and that there was a decrease in the size of dilatation in each succeeding pregnancy. Prather (1943) discussed this paper, and showed on the screen before the meeting several series of x-ray films from successive, normal pregnancies in women. These cases demonstrated that the dilatation of the renal pelvis and upper ureter does not increase, but rather tends to become less in each subsequent pregnancy. He concluded that the anatomical findings in monkeys are consistent with the changes we see in obstetrical patients.

MacLean and Deming (1943) reported a series of 68 cases of infection in pregnancy. They found that nearly two-thirds of all cases of infection occurred in the first and second pregnancies. These and other studies substantiate our original statement that if our experimental findings are consistent with human pregnancy, infection should be much less frequent after the first pregnancy. This is due to the fact that upper urinary tract drainage is improved after the first pregnancy.

What is the clinical value of this experimental work? Its value is to warn us that most urinary tract complications of pregnancy will occur in the first pregnancy. Previously unrecognized congenital anomalies and other pathologic lesions may be aggravated by the urinary tract stasis in pregnancy. With this knowledge, we recommend the study of the upper urinary tract before pregnancy. If this is not possible intravenous urograms should be done early in the first pregnancy. Thus we should be able to anticipate trouble before it arises and make pregnancy safer by appropriate therapeutic measures.

The understanding of the physiological reaction of the pelvis and ureter in successive pregnancies is of great assistance in the treatment of second and third pregnancies in women, who previously developed pyelitis in their first pregnancy. The opinion was generally held that if the first pregnancy were complicated by *pyelitis the second pregnancy, when allowed to continue, would be associated* with more serious complications. Unfortunately this opinion is still held by many. We may now predict that, in a second or third pregnancy, complications are less likely to develop, provided there is no pathological lesions of the upper urinary tract. Our clinical experience in treating these cases has confirmed this statement.

CONCLUSIONS

The physiological pyelo-ureteral dilatation of pregnancy is dependent upon the endocrine function of the placenta.

Most upper urinary tract complications occur in the first pregnancy, because stasis is greater at this time. Previously unrecognized congenital anomalies, which are frequent, and other pathologic lesions may be aggravated by the urinary tract stasis during pregnancy. With this knowledge, we recommend the study of upper urinary tract, by intravenous urograms, before pregnancy. If this is not possible intravenous urograms should be done early in the first pregnancy. Thus we should be able to anticipate trouble before it arises, and make pregnancy safer by appropriate therapeutic measures.

Due to the fact that upper urinary tract drainage is improved after the first pregnancy, we may now predict that complications are less likely to develop in a *second or third pregnancy provided there is no pathological lesion of the upper* urinary tract. Our clinical experience in treating these cases has confirmed this statement.

Acknowledgement: The early part of this study was supported by a grant from the John and Mary R. Markle Foundation to the Department of Obstetrics and Gynecology, and the later work by the Nutrition Foundation, Inc. X-rays were made possible by a grant from the Fluid Research Funds of the Yale University School of Medicine to the Section on Urology.

789 Howard Ave., New Haven, Conn.

REFERENCES

Boland, B. F.: J. Urol., 49: 245, 1943.
MacLean, J. T. and Deming, C. L.: J. Urol., 49: 236, 1943.
Prather, G. C.: J. Urol., 49: 245, 1943.
van Wagenen, G. and Jenkins, R. H.: J. Urol., 42: 1010, 1939.
van Wagenen, G. and Jenkins, R. H.: J. Urol., 49: 228, 1943.
van Wagenen, G. and Newton, W. H.: Surg. Gynec. & Obst., 77: 539, 1943.
van Wagenen, G. and Jenkins, R. H.: Am. J. Obst. In press.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DISCUSSION

DR. A. KELLER DOSS (Fort Worth, Texas): We are again indebted to Dr. Jenkins and Dr. van Wagenen for bringing to our attention the effect of the hormone state for the pregnant woman on the ureter.

There seems to be sufficient evidence in the literature to support the thesis that pyelo-ureteral stasis accompanying pregnancy stems from two factors: 1) dynamic, in which there is atony and diminished peristalsis of the ureter incidental to hormonal influences encountered in pregnancy; and 2) mechanical, owing to the presence and relative position of the enlarged uterus pressing upon atonic ureters.

That pyelo-ureteral dilatation is most marked in the primipara is generally accepted. This, as suggested by Hundley, et al., may well result owing to better tone of the abdominal musculature which, in turn, accentuates the pressure of the enlarged uterus on the ureters. It might be further expected that ureteral dilatation in the multipara, even though some degree of ureteral dilatation resulted from preceding pregnancies, would become less marked as the number of pregnancies increase owing to abdominal wall relaxation, therefore lessening the factor of ureterine pressure.

Since the degree of obstruction is greatest in the primipara, it is natural to expect a greater incidence of pyelonephritis in this group, for stasis in the urinary tract is but a ticket to infection.

Dr. Jenkins has pointed out that an excretory urogram, if not a thoroughgoing genito-urinary investigation, would assist greatly in the prevention or at least in the management of genito-urinary problems which frequently arise to complicate gestation in the primipara. With this noble aim I am in full accord, yet there is much missionary work which must be done to convince the obstetrician and newly wed alike that a urologist must be consulted either prior to pregnancy or early in the first trimester.

Fortunately, infection in the "upper urinary tract," even in the presence of stasis, does not pose the problem it once did before the discovery and general use of chemotherapeutic and antibiotic agents.

DR. NELSE F. OCKERBLAD (Kansas City, Mo.): This work of Dr. Jenkins and his group is extremely important, and I want to commend his industry in pursuing the subject. I feel that he has proved the hormonal theory of dilatation of the ureter in the pregnant state.

I wish to make one observation and that is, the younger the pregnant woman, the greater the amount of widening of the ureter.

Just because we have antibiotics and other means of combating infection, is no reason why we should consider the subject as completely solved. I hope that out of this work will come an antidote to the hormonal disturbance which causes the widening.

DR. JOHN T. MACLEAN (Montreal, P. Q.): I should like to congratulate Dr. Jenkins and Dr. van Wagenen on an excellent paper. They have made some interesting observations. They state that they consider pyelo-ureteral dilatation to be the predisposing cause of pyelonephritis, and recommend the early investigation of the urinary tract.

(Slide) I should like to draw your attention to this graph, which indicates the work of Dr. Deming and myself, referred to by Dr. Jenkins. This shows, first of all, the excretion of the hormones in the urine during pregnancy. In the early part of the pregnancy there is a very marked output of gonadotropic substance which drops off rapidly at the third month, although the estrins and corpus luteum hormone continue to be secreted in the urine until term is reached when they suddenly drop.

Dr. Jenkins and Dr. van Wagenen have shown that when the fetus is removed from the uterus, the excretion of hormone continues and dilatation of the ureter continues, and that is exactly what one would expect, since at this time, at approximately the third month,the placenta takes over the excretion of these two hormones.

If one uses Dr. Kretschmer's figure on the incidence of dilatation of the ureter, 52 per cent up to 5 months, shown by the blocked-off area, and 92 per cent up to 9 months, one finds that parallels exactly the increased excretion of estrin and corpus luteum hormone.

If you do one more thing, and superimpose on that chart the incidence of infection during the pregnancy, you find it increases as the pregnancy does, with the maximum at approximately the sixth month; in other words, the incidence of infection parallels exactly the increased incidence of dilatation of the ureter, which, in turn, parallels the increased excretion of estrin and corpus luteum hormone.

(Slide) Dr. Jenkins and Dr. van Wagenen state that they predict that the majority of infections would occur in the first and second pregnancies. This table, taken from our clinical work, indicates that this is true, with approximately $\frac{2}{3}$ of the injections taking place in the first and second pregnancies.

Dr. Ralph H. Jenkins (New Haven, Conn.): I shall take this opportunity to show a few slides I planned to show earlier.

(Slide) This film represents the first, second and third pregnancy of the same animal. The pictures were taken on the one hundred and fifty-eighth day of each pregnancy. It is noted that the ureteral dilatation tends to regress in each successive pregnancy.

(Slide) This film represents the first and second pregnancy in another animal at about the same day, showing decrease in the size of ureteral dilatation in the second pregnancy.

(Slide) The picture on the left represents a 4 months' normal pregnant animal showing the fetus, and no ureteral dilatation. The picture on the right shows the animal in the fifth month of pregnancy, with ureteral dilatation.

Following this examination, the fetus was removed and the placenta allowed to remain.

(Slide) The film on the left was taken a few days after operation, showing greater dilatation of the ureter, outline of the placenta can be seen. The film on the rightwas taken a few days after the placenta had been spontaneously, expelled, showing the ureters returning to normal. The fetus, in this case weighed 5 times as much as the placenta.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

ALLERGY OF THE PELVIC URINARY TRACT IN THE FEMALE: A PRELIMINARY REPORT[1]

LLOYD KINDALL AND THOMAS T. NICKELS

From the Urology Service, The Samuel Merritt Hospital, Oakland, California

Allergy does occur in the urinary tract, is frequently unrecognized, and generally mistreated.

Living in a community with a nationally known allergist, we have become allergy conscious. What is allergy? It is a composite of altered energy, an artificial word created by von Pirquet in 1906.

Recent medical dictionaries define allergy as "a condition of unusual or exaggerated specific susceptibility to a substance which is harmless in small amounts for the majority of members of the same species." It lists 14 subheadings. For simplification, these substances may be anything taken by mouth, subcutaneously, intravenously, or contact with any material substance or anything air-borne, but the most frequent offenders in the urinary tract are food and drugs.

ANATOMY

There are two longitudinal muscle layers in the ureter and between them a circular muscle layer. The circular layer is well developed in the upper ureter while the longitudinal muscles are small. Proceeding down the ureter, the circular layer becomes very small, while the longitudinal layers become larger. The ureter loses the circular fibers on entering the bladder wall, leaving the internal longitudinal layer, which gradually disappears in the bladder wall, while the outer longitudinal muscles extend through the trigone, under the internal sphincter of the bladder, and ends in the urethra.

The trigone muscle is a definite entity arising from the longitudinal muscle fibers of the ureters and superimposed on the muscles of the bladder wall. These fibers lie internal to the other muscular coats and spread out in fan-shaped arrangement decussating with those from the opposite side, some of them extend through the vesical orifice into the urethra.

On cystoscopic examination, it is this additional layer of muscle fibers which gives the trigone the appearance of being slightly elevated above the surrounding bladder wall. This arrangement may be partially responsible for the fact that increased ureteral irritability and activity are usually associated with irritability of the bladder, and result in the symptoms of urinary urgency and frequency. In the trigone, the submucosa is thin and the mucosa is closely attached to the muscularis, so that it is always smooth, even in the empty state.

Textbooks describe three points of narrowing in the ureter, the longest being the intramural portion, with no mention of the diameter of the ureteral meatus. Campbell Begg, in clarification of the cystoid theory of Fuchs, stated that there was from one to four constricted areas of the ureter, excluding the constant point of narrowing at the ureteral meatus, and that peristalsis will carry on on a myogenic basis.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

It has been generally believed that the ureter has an intrinsic neural mechanism and functions automatically through this mechanism, initiating and perhaps regulating its own muscular contractions. Lapides, in his recent work on the physiology of the intact human ureter, with catheters in the ureter, says: "It is possible to learn that tonus and rhythmic contraction of the intact human ureter are independent of the central nervous system, including the autonomic nervous system and its ganglia, and that the normal adequate stimulus for the initiation and maintenance of ureteral peristalsis is a stretching of the smooth muscle fibers of the ureter by the urine from the kidneys."

SYMPTOMS (SUBJECTIVE)

The symptoms of dysuria and frequency are due to irritability of mucous membrane of the trigone, superimposed on the longitudinal muscles.

Symptoms of pain are due to an allergic edema of the mucous membrane of the ureter or urethra, interfering with free drainage of urine into the bladder or through the urethra and causing spasm of the longitudinal muscles.

In chronic cases there may be a narrowing of the urethra at any point, due to a stricture, or to a submucosal infiltration of mononuclear cells associated with hypertrophy of the underlying muscle layers.

It is possible for an individual to have allergic phenomena of the ureter, producing ureteral pain on the basis of hypertrophy of the mucous membrane, submucosa and underlying musculature, with additional allergic edema at the site, which in addition, could produce lower urinary tract symptoms with no demonstrable lesion of these portions of the urinary tract.

Repeated episodes of allergy in the urinary tract and subsequent production of hypertrophied mucous membrane, submucosa, and underlying smooth muscle (as seen in the bronchi with an allergy state), with subsequent episodes, producing edema and irritation of the areas, could account for cases of ureteral pain with no allergic phenomena taking place in the ureter.

Symptoms may vary from mild cystitis with dysuria, frequency, and nocturia 0 to 1 times, to a severe type of urgency, frequency and sometimes terminal hematuria and frequent nocturia. Either of these conditions may be associated with urethral or ureteral pain. Psychic factors are an important consideration in the predisposing, precipitation and maintaining of allergic diseases.

SYMPTOMS (OBJECTIVE)

The urine sediment in mild cases contains only an occasional white cell, with no bacteria, as elicited by culture or stain. However, the occasional white cell, after proper centrifuging and treatment with Wright's stain, will show mononuclear leukocytes and frequent eosinophiles. In chronic cases, the urine sediment may show polymorphonuclear leukocytes, bacteria, as well as eosinophiles and mononuclear leukocytes.

We have been obtaining an Addis count with a differential of the stained sediment. In the three cases in which we have used this differential count (before and during an allergic state of the bladder) the percentage of mononuclear leukocytes in that group was 90 per cent. In 3 cases of normal individuals, giving negative histories of previous allergy in any system of the body, the differential ran 80 per cent polymorphonuclear leukocytes. As an additional diagnostic procedure, we suggest that further study of the Addis count with a differential of the stained sediment be done.

The mucous membrane of the urethra is frequently edematous and dusky red in color. There may be a narrowing in any part of the urethra.

The bladder neck may have the general appearance of polypoid reaction with a thickened mucous membrane, the surface of which may be irregular and the mucous membrane appear opalescent in character. The mucous membrane of the bladder may vary from slightly thickened appearance with surface somewhat irregular, pale pink and opalescent, to a more definite scattered nodulation of a dull pink color with increased surrounding vascularity, on to an actual superficial ulceration with overlying yellowish grey slough. There may be ecchymotic as well as hyperemic patches.

Either ureteral orifice may be swollen and edematous. The passing of a ureteral catheter may be difficult and will generally reproduce pain in the lower ureter. Bilateral retrograde pyeloureterograms are within normal limits.

History of allergic phenomena of other systems of the body is important. When allergy is suspected as the cause of pain in the lower ureter (irrespective of urine findings) and a blood smear shows a shift to the right, the patient is entitled to an intravenous injection of one minim of a 1–2600 solution of epinephrine, or 5 minims subcutaneously. Within 2 minutes following the intravenous injection, the patient will get marked relief of her symptoms, and within 5 minutes following subcutaneous injection. This test alone will prevent many unnecessary laparotomies.

While many case reports could be given, the following show many of the usual findings:

CASE REPORTS

Mrs. G., aged 43, was seen because of a dull pain in the right flank and right lower quadrant, associated with dysuria and frequency. The urine was negative; urograms showed a marked ptosis of right kidney. The patient was relieved when fitted with a corset and pad for support of her right kidney.

Six months later she had two "gin" punches, within 2 hours dysuria, frequency and pain developed in the right lower quadrant. About 6 hours later she had a dull pain in her right flank. When examined 48 hours later she was free of symptoms. As a therapeutic test 2 weeks after this, she was asked to take two "gin" punches the evening before coming to the office. There was a recurrence of all her symptoms. Cystoscopic examination showed many hyperemic areas in the mucous membrane of the bladder, and between the lesions the membrane appeared pale pink and opalescent. Around the right ureteral opening, the mucous membrane was edematous. Urine spurts from this opening averaged two per minute. Subcutaneously, the patient was given 5 minims of a 1-to-2600 solution of epinephrine. In 12 minutes the hyperemic areas in the bladder mucosa had completely disappeared and the spurts of urine from the right ureteral opening had increased to 9 per minute. They were of longer duration and with increased visualization within the ureteral opening. Patient was relieved of all pain.

Mrs. K., aged 44, was seen because of a sudden severe attack of left renal colic, with vomiting, and required morphine for relief. There was no history of previous attacks, hematuria or bladder trouble, and she had felt well until the onset of dull left mid-and lower abdominal pain associated with slight dysuria and urinary frequency.

A catheterized specimen of urine showed nothing abnormal. Her contracted urethra was dilated with a 26 F. sound. She was placed on oral therapy of ephedrine, $\frac{3}{8}$ gr. with a barbiturate, and within 12 hours her pain had disappeared. Eight hours after discontinuance of the ephedrine, the pains in her left mid-abdomen reappeared, more severe, and constant in character. The following day she was admitted to the hospital and given $1\frac{1}{2}$ gr. of barbiturate by mouth, and morphine gr. $\frac{1}{6}$ with atropine gr. $\frac{1}{200}$ hypodermically. At cystoscopy three-quarters of an hour later she was drowsy, but the pain persisted. Mucous membrane inside the urethral meatus was slightly edematous and of dull dusky red color.

A 24 F. cystoscope passed with some difficulty to the bladder, the capacity of which was 200 cc. The mucosa of the bladder appeared to be slightly edematous with absence of its normal glistening appearance. Over the trigone, the left lateral bladder wall and around the left ureteral meatus were many small hyperemic patches. Between these the mucous membrane had an opalescent appearance. A biopsy was taken within the edge of the trigone.

Intravenously, 1 minim of a 1–2600 solution of epinephrine was given. Within 2 minutes the left abdominal pain had completely disappeared. In 15 minutes, the bladder mucosa had assumed a normal appearance and the spurts of urine from the left ureteral orifice that had averaged about 2 per minute now increased to 7 per minute, were larger in caliber, longer in duration and there was increased visualization within the ureteral meatus.

Biopsy of the tissue taken before cystoscopy showed moderate mononuclear cell infiltration beneath the squamous epithelium and moderate edema of the mucous membrane. No eosinophiles were found. Section of the bladder mucosa showed eosinophiles and mononuclear leukocytes. Urine sediment contained an occasional white blood cell and Wright's stain revealed them as mononuclear leukocytes.

The patient was given ephedrine and referred to an allergist for further study. His report was that she was sensitive to many foods.

Cystoscopy 1 week later showed a lessening of the allergic phenomena in the mucous membrane and her subjective symptoms. After the sixth weekly cystoscopy the bladder showed normal appearance, and the patient was free of urinary symptoms.

DIAGNOSIS

1) Appearance and biopsy findings of the urethral and bladder mucosa Biopsies all show mononuclear cell infiltration and frequently many eosinophiles These biopsy findings are similar to those in cystitis follicularis and bladder neck polyps, which suggest the possibility that both these conditions are allergic in origin.

2) Urine sediment in early cases may show an occasional white cell, and when treated with Wright's stain, are shown to be of mononuclear type. In early cases urine culture and stain are negative for bacteria. In chronic cases the urine sediment may contain many polymorphonuclear leukocytes as well as bacteria. An infectious process may be imposed on an existing allergic state or the allergy may be secondary to toxemia of the infection.

3) Blood smear will generally show an increase in the mononuclear leukocytes and a decrease in the polymorphonuclear leukocytes. The percentage of eosinophiles is frequently increased.

4) Skin testing is unsatisfactory as a positive diagnostic aid since some foods give positive reactions though not causing symptoms, while causative foods may give negative reactions.

5) Therapeutic test is to reproduce the symptoms by giving the patient the suspected substances and then relieve the symptoms by use of epinephrine or ephedrine.

TREATMENT

1) Remove suspected agent responsible for the allergic attack.
2) Dilatation of the urethra.
3) Dilatation of the ureter and ureteral meatotomy when necessary.
4) In acute attacks administration of ephedrine and a barbiturate.
5) Antibiotic and chemotherapy for complications.
6) Restrict intake of fluids during attacks of pain.

SUMMARY

Allergic reactions do occur in the urinary tract. They are frequently undiagnosed and mistreated by injection of irritating chemicals. The allergic phenomenon in the urinary tract is a new field in urology, and certain pathological conditions will cause controversy because of the confusion existing in the field of allergy. Consideration of this concept is justified as an aid in the management of many cases which do not fit into any accepted categories.

Symptoms and reactions which have been reproduced have been relieved with this outlined treatment.

Biopsy and urinary findings are reported and an explanation of allergic symptoms is given.

We desire to express our appreciation to Dr. Charles Baker, pathologist, Samuel Merritt Hospital, Oakland, California, for his interpretation of pathological and laboratory material.

400—29th St., Oakland 9, Calif.

REFERENCES

BEGG, R. C.: Physiological variations in pyelograms commonly interpreted as pathological. A revised standard of normality with special reference to "cystoid" theory. Brit. J. Urol., 18: 176, 1946.

EVERETT, H. S.: Gynecological and Obstetrical Urology. Baltimore: Williams & Wilkins, 1944.

HINMAN, F.: Principles and Practice of Urology. Philadelphia: W. B. Saunders Co., 1935.

LAPIDES, J.: The physiology of intact human ureter. J. Urol., 59: 501, 1948.

LEWIS, B.: J. Urol., 15: 189, 1926.

McCREA, L. E.: Clinical Cystoscopy. Philadelphia: F. A. Davis Co., 1945, vol. 1.

ROWE, A. H.: Clinical Allergy due to Foods, Inhalants, Contactants, Fungi, Bacteria and Other Causes: Manifestations, Diagnosis and Treatment. Philadelphia: Lea & Febiger, 1937.

——: Elimination Diets and the Patient's Allergies. Philadelphia: Lea & Febiger, 1944.

——: Personal communication to authors, 1948.

SATANI, Y.: Histologic study of the ureter. J. Urol., 3: 247, 1919.

URBACH, E. AND GOTTLIEB, P. M.: Allergy. New York: Grune & Stratton, 1946, 2nd ed.

WESSON, M. B.: Anatomical, embryological and physiological studies of trigone and neck of bladder. J. Urol., 4: 279, 1920.

The Journal of Urology
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DISCUSSION

Dr. Fred K. Garvey (Winston-Salem, N. C.): I fear that any discussion by me on this interesting and extremely important subject will be most hypothetical and most certainly not enlightening. It is a subject that I am sure most of us have been, in a superficial way, cognizant of but for various reasons have not had the courage or strong enough conviction to pursue its study as Dr. Kindall has.

Cysto-urethritis is an age-old term for a very common condition in the female. It has never been thoroughly understood but usually has been amenable to simple office procedures. The most commonly accepted etiology of inflammatory-like reactions of the posterior urethra and trigone in the female is that of infection of the glandular structures of the vesical neck. This may have occurred in infancy, childhood, beginning of sexual life in the form of marital cystitis; from trauma of the posterior urethra incident to childbirth; infection from postoperative catheterization, secondary infection from the upper urinary tract, and so forth.

The splendid work of Folsom and others demonstrating "the female prostate," based on the female urethra being homologous to the posterior urethra in the male has been accepted by many as the answer to the problem of cysto-urethritis in the female. This, and the ease with which these patients are symptomatically relieved by instrumentation and silver nitrate applications, have caused most of us to be complacent and not to do thorough differential studies before accepting the diagnosis and instituting treatment.

Probably all of us are familiar with the typical case that comes to us with a history of intermittent attacks of frequency, urgency and burning or even dysuria in which we find the urine to be normal but, on passing an endoscope, we find redness and edema of the vesical neck and most likely of the trigone. There is usually found a certain amount of narrowing of the urethra which is either due to edematous thickening or mild stricture formation. Passage of the cystoscope occasionally gives complete relief in these cases, but usually passage of sounds of larger caliber is necessary to bring about relief.

The mild, bullous edema occasionally seen not only around the vesical orifice, but along the ureteral ridges of the border of the trigone would indicate that both conditions are from a common source and I think can frequently be accounted for by an allergic manifestation. Certainly the polyp-like projections which we commonly see around the roof of the vesical neck would to me indicate allergy in that it is well known among rhinolaryngologists that most polyps in the nose are due to allergy.

To me the most intriguing feature of Dr. Kindall's study is his findings in the urine sediment and in his biopsy of the bladder mucosa and musculature. It had never occurred to me to do Wright's stain[1] on the urine with only an occasional white cell as did Dr. Kindall when he found that mononuclear leukocytes and eosinophiles are frequently present. I think this finding is the strongest point in favor of allergy. The finding of mononuclear leukocytes and eosinophiles in his biopsy as well as an increase in the mononuclears and eosinophiles in the blood smear has considerable weight toward there being an allergic state present.

I strongly suspect that Dr. Kindall, even though the cases he reports are apparently extrinsic allergy, mainly due to foods, will find many of them may be of the intrinsic type in which there is no known allergy manifestation elsewhere and no sensitivity to foods, that many of these cases are due to histamine sensitivity and are precipitated by emotional upsets of various types. Also many may be on a bacterial basis with histamine reaction on the blood vessels very much as occurs in vascular headaches.

Since reading his paper, I am stimulated to try treatment on some of my ever-recurring cases with ephedrine or pyrabenzamine, or even adrenalin, and, if relief is obtained, to follow this with histamine tests. I suspect that Dr. Kindall has given this a trial or at least considered it, and should like to ask him to discuss this phase of the condition in closing. I should also like to ask him if he has tried etamon in any of his cases.

I have discussed this matter of urinary allergy with Dr. George Harrell, Professor of Medicine, of the Bowman Gray School of Medicine, who states that he has 2 cases of food allergy in which the allergen in each case always produces urinary frequency and burning. This is relieved by antihistaminic agents but no cystoscopic studies have been made on either case. I have 1 case of food allergy in which the same phenomenon occurs without any abnormal findings in the urine.

Duke, in his report in 1922, relating his experiences testing for specific hypersensitiveness of obscure medical cases, stated:

"Bladder allergy is not a rare cause of bladder trouble, but is a relatively common one particularly in the group of patients with bladder disturbances who exhibit little or no pathology in the urinary tract to account for it."

Miller and Uhle in 1939 reported 2 cases of renal colic without subsequent evidence of upper urinary tract disease one of which was associated with urticaria. Adrenalin given hypodermically relieved both the pain and the urticaria in one case, and the pain in the other, with prompt relief.

Various workers have sought an explanation of the lower urinary symptoms occurring in patients with normal urine demonstrating only a trigonitis. Mann's theory that an abnormal state of the urine may irritate the urinary tract, has been considered and experimental work done on this by Dr. Henry L. Douglas which was reported in 1940.

Matthews suspected that in the oxidation of amino acids, amines of highly toxic character are produced in certain individuals. This was thought possibly to be due to the action of bacteria. Dr. Douglas ran a goodly number of cases using sodium ricinoleate to detoxify the colon attempting to minimize the absorption of putrefactive products in the intestinal tract. The results were variable but interesting.

I think we must consider estrogen deficiency as an etiologic factor in certain cases since we see changes in the urethra and bladder around menopause which are ameliorated considerably by the use of stilbesterol or other forms of estrogen.

I certainly enjoyed Dr. Kindall's splendid paper and feel that he has not only gone a long way toward explaining the cause of a good percentage of the cases of urethrocystitis and ureterospasm, but also may stimulate more careful study and consideration by the urologic profession in general in their diagnosis and management of this very common condition. That he is pioneering in this work is evidenced by the paucity of studies on allergy in the urinary tract, as reported in the literature. I wish to congratulate him on this work and eagerly await his further reports on this study.

DR. ELMER HESS (Erie, Pa.): It seems interesting to me that there have been two avenues of approach to the conclusion that there are allergic manifestations involving the urinary tract. There have been allergic-minded individuals such as a nose-and-throat friend of mine who said, "I don't know anything about urology, but it is obvious to me that if urologists don't recognize allergic reactions in their territory, it is just because they aren't looking for them."

The other approach is typified by the man who says, "Good Lord, we've ruled out everything else in this case except allergy and chestnut blight, maybe it's one of those."

It seems probable that the allergist calls too many conditions "allergies," while the skeptic sees too few. Our own approach has been a bit unscientific, since it has been strictly empirical. We have seen a good many cases, in both male and female, where there has been diffuse or patchy erythema or even exudative inflammation of the mucosa of the urinary tract, in which cultures, both aerobic and anaerobic, on a variety of media fail to yield any organism. By failure of the therapeutic test with arsenicals, it has been concluded that they do not fall in the group of abacterial pyurias.

Since virtually every patient somewhere along the line, says: "Doctor, could it be something I eat?" we have been gradually forced into wondering the same thing. Some patients have found a partial answer for themselves and will volunteer the information that tomatoes, or strawberries, or some other specific food may be relied on to bring about an attack.

I should like to be able to report that we have done detailed studies on the urinary sediments and have been otherwise astute in our observations, but we have not. Instead we have simply tried the use of antihistaminic agents such as pyrabenzamine, benydryl, or histadyl. The results have not been uniform, but there have been enough examples of striking relief on this therapy, when nothing else has helped, to make us feel that there is a solid basis for further study.

DR. J. S. EISENSTAEDT (Chicago, Ill.): I had not prepared any discussion on this subject but I am very much interested in it and wish to thank Dr. Kindall for bringing it to our attention. Very little has appeared in the American literature, in fact there is very little in the English language on the subject of urinary tract allergy. I wish to report briefly a few cases which I think fall well within the group particularly if we accept the wider interpretation and definition of allergy.

Two of the patients were wives of physicians and our approach to diagnosis was carried out much like in the second group that Dr. Hess commented on. We attempted to rule out every other possible cause for urinary difficulty. One woman showed allergy or sensitivity, and the two terms are really not synonymous, to codeine. The symptomatology in her case was quite different from that in the cases which Dr. Kindall reported. When codeine was given in a cough mixture or for any other purpose she had an attack of renal colic with the presence of red blood cells in the urine. This has been repeatedly observed in this patient. She was sent to an allergist after every other means of examination was used and all our findings in a complete urological study were negative except for the presence of the red blood cells in the urine. A day or two after the cessation of the use of codeine all symptoms disappeared.

The other patient showed a marked allergic reaction to the fermentation products of milk as evidenced by dangerously severe reaction after the ingestion of Roquefort cheese. Her symptoms were identical with the other doctor's wife and she has remained well after abstinence from known allergens.

Another patient who has been followed by one of our colleagues present here is the superintendent of a dried milk plant for large dairy interests and it has been shown definitely, at least to my satisfaction, that the hematuria of which he complained was due to the effect of milk even when minute particles of dried milk were inhaled at the time of inspecting these plants. Eventually he was provided with white cotton suits and caps and naturally the avoidance of all milk products by mouth was carried out. After this his urine showed marked improvement but still contained microscopic blood. After the use of a filter which he wore in the plant on inspection tours, his urine cleared completely and there was no more microscopic blood found. I have had three other cases of urinary tract allergy in which multiple allergens were demonstrated.

DR. LLOYD KINDALL (Oakland, Calif.): I want to thank Dr. Garvey, Dr. Hess and Dr. Eisenstaedt for their remarks.

There are several references in my paper of biopsy findings of bladder and urethral mucosa.

In 1926 Bransford Lewis wrote an article in which there was reference to referred spasm and pain in the trigone and in the lower ureter from partial bladder neck obstructions in both men and women. Anything that irritates the thin mucosa overlying the longitudinal muscles of the trigone will produce a reflex pain in the urethra. It is a crime to instill any type of irritating chemicals into the bladder.

Reviewing the anatomy of the ureter, the longitudinal muscles are largest where the ureter enters the bladder wall. Anything that produces an edema of the mucous membrane in the intramural portion of the ureter, and more particularly the ureteral meatus, will prevent the free flow of urine into the bladder and produces a spasm of the longitudinal muscles of the ureter which frequently causes pain in the lower ureter, trigone and urethra.

Edema of the ureteral meatus is easily and readily recognized with the cystoscope. A patient having pain in the lower ureter, with edema of the ureteral meatus may be given 1 minim of epinephrine intravenously, or 5 minims subcutaneously and in a few minutes the patient will voluntarily say: "Why Doctor, the pain is gone".

After giving the epinephrine, the ureteral spurts of urine, which were 1 or 2 per minute, will increase within 2 minutes to sometimes 6 or 8, or 10 per minute. The spurts of urine are of much longer duration and you get an increased visualization in that ureteral opening. The use of this procedure will prevent many unnecessary laparotomies.

THE JOURNAL OF UROLOGY
Vol 61, No 2 February 1949
Printed in U S A

NORMAL AND ABNORMAL MICTURITION A STUDY OF BLADDER BEHAVIOR BY MEANS OF THE FLUOROSCOPE[1]

S RICHARD MUELLNER AND FELIX G FLEISCHNER

From the Departments of Urology and Radiology of the Beth Israel Hospital, Boston, Mass

I NORMAL MICTURITION

In the course of an investigation of the problem of stress incontinence in women, it occurred to one of us (S R M) to study bladder behavior under the fluoroscope Micturition as we saw it on the fluoroscopic screen appeared to be at variance with some of the established concepts of the physiology of this process

We therefore proceeded to verify our findings by observing micturition in men, women and children, in normal individuals as well as in patients in whom it was altered either by obstructive or neurogenic disease To date, more than 100 observations have been made As is so often the case, we found eventually that fluoroscopy of the bladder was not original with us, but that it had occurred independently to Blum and his co workers and to Boeminghaus Unfortunately however, these authors failed to exploit fully this method of study, and merely limited their observations to the changes in bladder shape during micturition

Our technique of bladder fluoroscopy is briefly as follows (fig 1) The bladder is first filled through a 16 F catheter with a contrast medium and the catheter is then withdrawn At first we used a 13 per cent solution of sodium iodide, to which one ampule of aquaeous diodrast (20 cc, 35 per cent by volume) had been added Later on we found that a 5 per cent solution of sodium iodide gave an equally satisfactory shadow when combined with the diodrast If greater density of the bladder shadow is required in obese patients, an additional ampule of diodrast may be added to the mixture, or the strength of the iodide solution may be increased

A bladder filling of about 200 cc is usually sufficient for study in the average case In neurogenic vesical disturbances, however, a much larger bladder filling may be necessary and it is often advisable to observe the bladder while it is being filled Observations are made while the subject is supine, and when turned to one side or the other Care must be taken to maintain the relationship of the x-ray tube to the symphysis pubis, so that changes in the position of the bladder resulting from a change of posture can be accurately evaluated

The fluoroscopic table is then raised to the vertical position and the events at the beginning of micturition, while it proceeds, and when the stream is voluntarily inhibited, are carefully noted Spot films of the various phases of micturition are taken from time to time A special plastic urinal which would not cast an x-ray shadow was devised, to permit the subject to void while standing (fig 2)

Our present concept of the physiology of micturition has been summarized

---

[1] Read at annual meeting, American Urological Association Boston, Mass , May 18, 1948

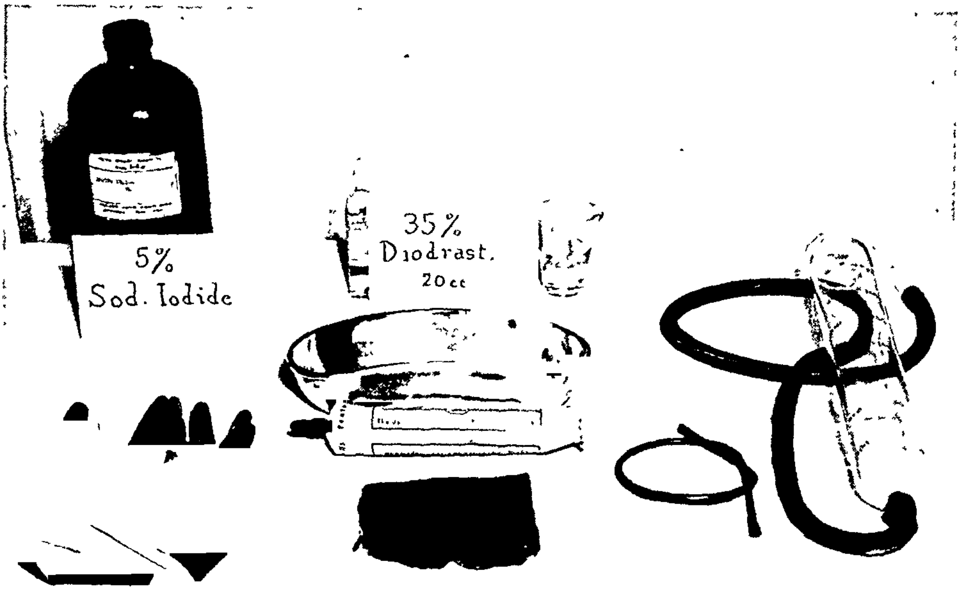


FIG. 1. Materials needed for bladder fluoroscopy: 5 per cent solution sodium iodide, one ampule of Diodrast, sterile gloves, a sterile catheter (16 F.), lubricant, and a gravity tube.

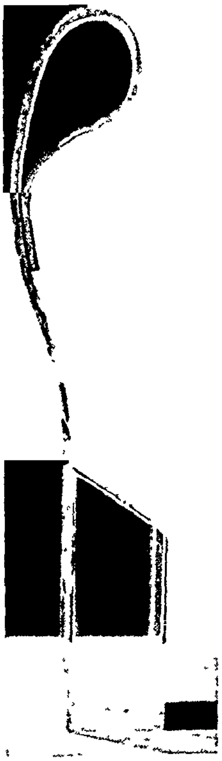


FIG. 2. Plastic urinal. Note long handle

by Langworthy as follows: "Micturition is initiated by a contraction of the vesical muscle itself. It is only after this contraction is well under way that the vesical orifice opens and then the external sphincter relaxes. Neither can be opened voluntarily. The vesical orifice opens following voluntary contraction of the detrusor. It is possible to close the external sphincter, which leads to subsidance of vesical contraction."

Voluntary micturition and deliberate inhibition of the urinary stream as seen under fluoroscope, however, vary in important details from the above description.

Although the events are the same in both sexes, they are more easily discernible in the female because of the simpler structure of the urethra, and micturition in the nullipara will therefore be used as an illustration.

In the nulliparous woman the bladder has a smooth outline and its base lies just above the symphysis pubis when she is recumbent and when she stands up (fig. 3, *A*).

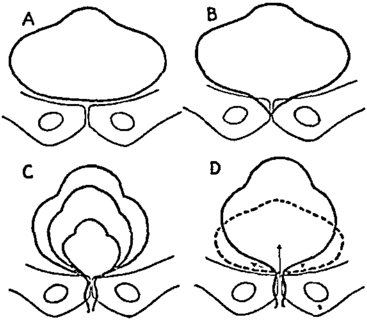


FIG. 3. *A*, Bladder of nullipara; patient in erect posture. Note smooth base line and its relation to symphysis pubis. *B*, Attempt at wilful micturition. Note descent of internal sphincter and pointed appearance of bladder base. *C*, [illegible] -shape during micturition. Level of internal sphincter [illegible] diminishes. *D*, To stop urinary stream, bladder base i[illegible] Urinary stream is shut off at level of internal sphincter. Dotted line, Bladder at rest.

When she is asked to void, she pulls the bladder base down sharply so that it descends rapidly and becomes "pointed" (fig. 3, *B*). This maneuver pulls the internal sphincter down. In some individuals one can see a small amount of the contrast medium enter the proximal urethra, and after a short but distinct lag the detrusor contracts and micturition ensues. The detrusor contraction, in consequence of the entrance of fluid in the urethra, would tend to confirm for man the second, third, and fourth reflexes which Barrington noted in cats. Such a clear cut sequence of events, however, is not common and in many subjects the mere sharp downward descent of the internal sphincter seems to be enough to precipitate the reflexes of micturition. When the detrusor contracts it rises up, so that its horizontal diameter becomes shorter and the vertical diameter longer. As micturition proceeds, the detrusor contracts centripetally and the internal sphincter, which was considerably lower in the pelvis at the beginning of micturition, gradually rises as the bladder volume diminishes (fig. 3, *C*).

When the subject is asked to inhibit the urinary stream, she invariably lifts the bladder base up sharply *so that it becomes horizontal and rises to a level* slightly higher than that of its resting phase. This "levelling" of the bladder base shuts the internal sphincter off, and one can see the detrusor gradually relax. Wilful cessation of urination therefore, seems to occur first at the level of the internal sphincter (fig. 3, *D*).

Micturition and interruption of the urinary stream in the normal male is brought about by the same mechanisms as in the nulliparous female. In the male it is rather surprising at first to see the very considerable mobility of the bladder base when the urinary stream is started or stopped. In the male the pointing of the bladder base at the beginning of deliberate micturition is not as marked as in the female, and manifests itself rather as a fairly deep dimpling in the region of the internal sphincter. The wilful interruption of the stream, however, is carried out by the same maneuver as in the female, so that the bladder base is rather sharply pulled up to become horizontal. At no time did we observe the urinary stream to shut off first in the region of the external sphincter.

DISCUSSION

It is quite obvious, from the description of voluntary micturition just presented, that the study of its physiology by means of the fluoroscope and its investigation by cystometry do not yield the same results. Cystometry has led to the conclusion that micturition is brought about by the direct action of the will on the detrusor. When the will has induced the detrusor to contract, the internal sphincter is then opened reciprocally, and *this in turn is followed* by the reflex opening of the external sphincter, and micturition thus proceeds.

Furthermore, for deliberate inhibition of the urinary stream, according to cystometry, it is the external voluntary sphincter which is contracted first to shut the stream off.

Fluoroscopy of the bladder, on the other hand, shows clearly that the immediate and direct effect of the will is not to contract the detrusor, but to depress the bladder base and to pull the internal sphincter way down. This maneuver either opens the sphincter, or precipitates the reflexes of micturition, for it is only after a distinct lag that the detrusor is seen to spring into action.

To shut off the urinary stream, the effect of the will is once more seen to manifest itself at the level of the bladder base, which is lifted way up, and thus stops micturition at the region of the internal sphincter.

The difference in result obtained by the two techniques of study has important implications. Bladder fluoroscopy reveals a distinct and separate mechanism for starting and stopping micturition, one which is interposed between the will and the detrusor. This mechanism which pulls the bladder base up or down is obviously located beneath the bladder and on the pelvic floor. A review of the anatomy of the muscles of the pelvic floor, and especially the excellent contributions made by Thompson, Savage, Holl, Lesshaft, and Smith make it quite clear that it is the pubococcygeus muscle, aided perhaps to a small degree by the deep transverse perinei muscle, which plays this important role. In the female the bladder base is intimately connected with the pubococcygeus through the medium of the endopelvic fascia In the male the prostate is interposed between the bladder base and this muscle, and moves up and down with the bladder base It is for this reason that the older anatomists sometimes referred to the pubococcygeus as the "levator prostatae"

The pubococcygeus, judging by its anatomic attachments, obviously cannot pull the bladder base and the internal sphincter down There is indeed no muscle in the pelvic floor or in the perineum which could do this

The descent of the bladder base is brought about by the deliberate relaxation of the pubococcygeus, aided by an increase in intra abdominal pressure, (a momentary fixation of the diaphragm at the end of an inspiration and a brief contraction of the abdominal musculature) at the beginning of micturition, and by gravity resulting from the erect or sitting posture The weight of the fluid in the bladder is not a factor, because the bladder base descends just as readily when it contains only a few ounces of fluid as when it is filled

Active contraction of the pubococcygeus, on the other hand, quite readily can lift the bladder base up

The voluntary mechanism for starting or stopping micturition is thus mediated entirely through striated (voluntary) muscle with a somatic innervation, (pudic nerve) and the assumption that the will directly affects the smooth (involuntary) muscle of the detrusor is therefore erroneous

The descent of the bladder base is manifested externally by relaxation of the perineum The relaxation of the perineum at the beginning of micturition has been noted by many investigators in the past, but its meaning has been misinterpreted Thus Denny-Brown believed it to be "an associated movement such as the movement of the ears when moving the eyes to one or the other side, or movement of the arms in yawning"

In summary then, wilful micturition in man begins with the co-ordinated action of the striated muscles of the pelvic floor, abdomen and diaphragm, of which the former is the most important The action of these muscles precipitates the reflexes of micturition by their downward push of the internal sphincter

It is only after this maneuver that contraction of the detrusor ensues Micturition is wilfully stopped by a sharp upward pull on the bladder base, which on introspection would seem to be brought about by the contraction of the levator ani (including the pubococcygeus) and which raises and levels off the bladder base so that the inhibition of the urinary stream appears to occur first at the level of the internal sphincter

II ABNORMAL MICTURITION

Having demonstrated that the voluntary mechanism initiated and stopped micturition, it now became desirable to know in what ways the pattern of micturition would be altered if the voluntary mechanism were eliminated

To demonstrate this point, a case of cancer of the prostate was chosen, in which the growth had fixed the gland in the pelvis The fixation of the prostate also fixed the bladder base so that it could neither be lowered nor raised

The voluntary mechanism was thus immobilized while the bladder nerves, however, were intact.

This patient, T. G., B.I.H. case No. 90794, aged 82, was known to have cancer of the prostate for the past 4 years. During the past year he had considerable frequency of urination, voiding about every 2 hours day and night. Micturition was characterized by marked urgency which he could not inhibit, and he had to have a urinal close at hand at all times. When he was asked to void deliberately, his efforts consisted of violent straining, and at times he succeeded in voiding a drop or two of urine (fig. 4). On catheterization the bladder residual amounted to 6 ounces.

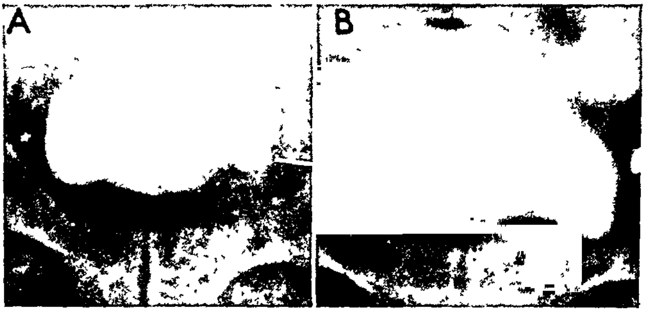


FIG. 4. Patient T. G. *A*, Bladder at rest. *B*, Attempt at deliberate micturition. Note immobility of bladder base and herniation of bladder towards obturator foramen as a result of straining.

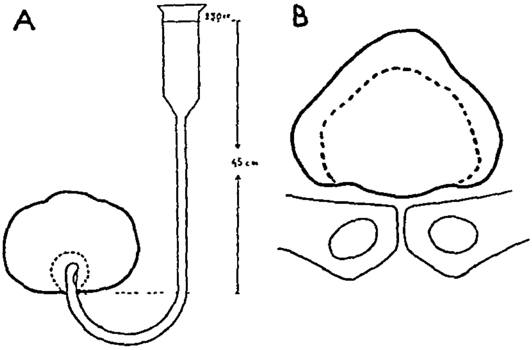


FIG. 5. Patient T. G. *A*, When filled to point of critical stretch, detrusor contracts and contrast medium is voided against atmospheric pressure of about 40 mm. mercury into gravity tube. Bladder empties almost completely. Dotted line shows residual. *B*, Detrusor filled to point of critical stretch and catheter removed. Voiding through rigid cancer-surrounded urethra, patient passes only 2 ounces, and residual of 6 ounces remains. A and B demonstrate effect of urethral resistance on detrusor efficiency in automatic micturition.

During the filling of his bladder with the contrast medium, the detrusor could be seen to expand gently until the point of "critical stretch" was reached. This occurred at a volume of 8 ounces. When this point was reached the detrusor could be seen to contract spontaneously and he voided all of the contrast medium back into the gravity tube which was held 1½ feet above the bladder level. His detrusor contraction thus was able to overcome an atmospheric pressure of approximately 40 mm. mercury (fig. 5, *A*). When the detrusor had relaxed the bladder was again gently filled to the point of critical stretch and the catheter was quickly withdrawn. The detrusor again spontaneously contracted for micturition, but having to void through the unyielding cancer-surrounded urethra which offered considerable resistance to the outflow of urine, only 2 ounces of the medium was passed, and the detrusor spontaneously relaxed (fig. 5, *B*).

During micturition the patient was unable to stop the stream although his membranous urethra and the external sphincter were not encumbered by cancer. At no time was he able to induce a willful detrusor contraction when his bladder was filled short of the point of critical stretch, despite the fact that his bladder nerves were intact.

This case demonstrates a few important points. It shows quite clearly that the elimination of the voluntary mechanism abolishes the ability to induce and to stop micturition. The will in this case was powerless to get the detrusor to contract, nor could it shut off the external sphincter until the detrusor had relaxed spontaneously. Micturition thus becomes entirely automatic once the voluntary mechanism is knocked out.

In automatic micturition then, the entire act of emptying the bladder is taken over by the detrusor which contracts spontaneously once it has been filled to the point of critical stretch. This impending detrusor contraction is signalized as an urgent desire to void, and can neither be induced nor inhibited by the will. It is quite clear from the above experiment that the ability of the detrusor to empty, will to some extent depend on the urethral resistance to the outflow of urine. The degree and the rate of development of urethral resistance must therefore in some measure have direct bearing on the size of the bladder residual.

The difference in volume between the fixed residual and the point at which critical stretch occurs determines the frequency of urination in a patient with an automatic bladder. Thus in the patient T. G., the fixed residual amounted to 6 ounces. The point of critical stretch occurred at a filling of 8 ounces. He thus voided whenever two ounces of urine had accumulated on top of his residual.

The development of automatic micturition in a patient with cancer of the prostate who has an intact nerve supply was surprising, since in the past we were led to believe that bladder automaticity developed only after transection of the cord.

Micturition in the patient with cancer of the prostate was next compared with its performance in a tabetic (A. A., B.I.H. x-ray No. A13905); in a paraplegic (J. D., B.I.H. case No. 98662); in a patient with multiple sclerosis (L. G., B.I.H. case No. 78445); and in still another patient with diabetic polyneuritis and hemiplegia (S. L., B.I.H. case No. 943346). Here then, were 4 different types of "cord bladder," and it was reasonable to expect that micturition would be different in each case.

On fluoroscopic study *every one of these patients was found to have the same* automatic type of micturition that we saw in the patient with cancer of the prostate. These patients had only one thing in common, and that is, the flaccid paralysis of the muscles of the pelvic floor, and hence the abolition of the voluntary mechanism. Despite the great variation in the disease, each case nevertheless developed the same type of automaticity.

We are therefore forced to conclude that automatic micturition will invariably result, irrespective of the nature of the process which has excluded the voluntary mechanism, and that a cord bladder is therefore not invariably the specific disturbance caused by a particular nerve lesion that we believed it to be in the past.

This concept alters considerably the clinical approach to the problem of the cord bladder. Whenever the voluntary mechanism is abolished, the goal of therapy must then be to achieve as early as possible automaticity of micturition in a bladder of approximately normal capacity, with a minimum of residual and urinary tract infection. A small residual and an approximately normal bladder capacity are desirable, in order to achieve reduction of urinary frequency. Therapy would thus not become merely a choice between tidal drainage (Munro and Hahn), or resection of the vesical neck (Emmett) one to the exclusion of the other. The need for these and other measures can now be fairly accurately ascertained in each case, on the basis of specific determinations, which disclose the status of the voluntary mechanism, the status of the bladder, i.e., its capacity and tonicity, and the degree of urethral resistance to the outflow of urine.

SUMMARY AND CONCLUSIONS

Man has a distinct voluntary mechanism with which to start and stop micturition.

This mechanism consists of the pubococcygeus, a large, paired, striated muscle with a somatic nerve supply, aided by the diaphragm and the abdominal musculature.

Micturition becomes automatic if the voluntary mechanism is immobilized by organic disease such as cancer of the prostate, or by nerve lesions which produce flaccid paralysis of the muscles of the pelvic floor.

In automatic micturition, the bladder can empty its contents fairly well unless it has been allowed to deteriorate by overdistention, or become scarred by infection.

In the management of cord bladders the status of the voluntary mechanism, of the detrusor as well as the degree of urethral resistance to the urinary outflow, must be ascertained.

The goal of therapy in patients who have lost their voluntary mechanism must be the prompt establishment of automatic micturition in a bladder of nearly normal capacity, and with a minimum of residual and infection.

520 Beacon St., Boston, Mass.

REFERENCES

Barrington, F. J. F.: The component reflexes of micturition in the cat. Parts 1 and 2. Brain, 54: 177–188, 1931.

Blum, Von V., Eisler, F. and Hryntschak, T. H.: Zystoradiaskopie. Wien. clin. Wchnschr., 31: 677–680, 1920.

Boeminghaus, H.: Zur Cystographie der Menschlichen Hanblase. Ztschr. f. urol. Chir., 6: 92–105, 1921.

Denny-Brown, D. and Robertson, E. G.: On the physiology of micturition. Brain, 56: 149–190, 1933.

Emmett, J. L.: Further observations in the management of cord bladder by transurethral resection. J. Urol., 57: 29–41, 1947.
Holl, M.: Handbuch der Anatomie des Menschen. Jena: 1897, vol. 2.
Langworthy, O. R., Kolb, L. C. and Lewis, L. G.: Physiology of Micturition. Baltimore: Williams & Wilkins, 1940.
Lesshaft, P.: Ueber die Muskeln und Fascien der Dammgegend Beim Weibe. Morph. Jahrbuch., 9: 475–532, 1883–1884.
Munro, D. and Hahn, J.: Tidal drainage of the urinary bladder: A preliminary report on this method of treatment as applied to "cord bladders" with a description of the apparatus. New Eng. J. Med., 212: 229, 1935.
Savage, H.: The Female Pelvic Organs. Philadelphia: Lindsay and Blakiston, 1876, 3rd ed.
Smith, W. C.: The levator ani muscle: Its structure in man and its comparative relationships. Anat. Rec., 26: 175–203, 1923.
Thompson, P.: The Myology of the Pelvic Floor. Manchester, 1899.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DISCUSSION

DR. R. E. VAN DUZEN (Dallas, Texas): Drs. Muellner and Fleischner should be congratulated for this extensive and thorough fluoroscopic study of the act of urination in humans. It has been well controlled by frequent observations and "spot" films. They have demonstrated very well the pulling down of the region about the internal vesical orifice as the first phase in the act of urination. This is followed by a momentary "lag" and then an elevation of vesico-urethral juncture and shortening of horizontal diameter of the bladder. This corresponds to what we have previously described in humans and Rhesus monkeys. We have always insisted the act of micturition is due to active muscular contraction and not due to relaxation of the vesical orifice.

However, the fluoroscopic and x-ray shadows are only silhouettes and if deductions are made from these alone, they may be misleading. We insist one must combine these studies with cystoscopic, anatomical and experimental studies on animals (but not on dogs or cats) before one can draw deductions on the sequence of events. In 1936, before the Southern Medical Association, we described longitudinal fibers of the detrusor muscle which passed down on the lateral wall and interlaced with the circular fibers about the vesical neck. This study was made by making serial sections of the bladder neck of a 4 year old girl. Every tenth section was stained and with the aid of the reflecting microscope, these were projected on a screen at 40 feet. With this magnification, we were able to study the muscular arrangement satisfactorily. We also noted that if one observed the internal vesical orifice at about 4:00 and 8:00 o'clock "on the dial" cystoscopically, one sees often a lateral pull when the patient tries to urinate. This was not lost in cases who have had presacral neurectomy while in the same patients, the trigone muscle action was lost. This indicates that these fibers were innervated by the parasympathetics.

Drs. Muellner and Fleischner do not mention the action of the trigone muscle. We do not believe it can be disregarded. We realize it is a small structure. But if it has no important action, why do patients with obstruction at the vesical neck have hypertrophy of the trigone muscle? Why do women with injury to the trigone muscle and no injury to the circular fibers of the internal vesical orifice, have to strain to void and often show trabeculation of the posterior bladder? Why have we cured obstinate cases of enureses by section of the presacral nerve? The answer is that it is more difficult to open the internal vesical orifice when we lose the action of the trigone muscle.

We believe that the sequence of events in the act of micturition are:

1) Tilting of the pelvic planes as described by Rose. Simultaneously there is a contraction of the trigone muscle which depresses the posterior lip of the internal vesical orifice. Fluoroscopically it is shown by the depression of the floor of the bladder.

2) After a brief lag, there occurs contraction of the longitudinal fibers of the detrusor muscle which first opens the orifice laterally and then further muscular

contraction shortens the bladder in the longitudinal axis. This latter is so well shown by Drs. Muellner and Fleischner. When one stimulates the second sacral nerve in the Rhesus monkey, a contraction wave is seen to start at the bladder neck, the bladder becomes tense and the contraction wave rises toward the dome of the bladder. This is very suggestive of the systolic phase of the cardiac cycle. We believe that the longitudinal muscle fibers tries to pull the internal vesical orifice over the contents of the bladder, similar to what some obstetricians now feel occurs in labor when the uterine muscles attempts to pull the cervix over the presenting part.

Lastly I would like to again congratulate Dr. Muellner and Fleischner on their excellent contribution. They have shown in black and white and in a way never shown before that the act of urination is an active muscular action and not a relaxation of the internal vesical orifice.

DR. S. RICHARD MUELLNER (Boston, Mass.): I want to thank Dr. Van Duzen for his very able discussion of this paper. There are a few points we wish to emphasize in regard to the physiology of normal micturition. First, that man has a distinct voluntary mechanism, consisting of the pubococcygeus, a paired, striated muscle with a somatic nerve supply, with which he starts and stops micturition. The assumption current to date, that the will can directly cause the detrusor to contract or to relax, is a physiologic inconsistency. Involuntary muscle is not notably under the influence of the will. It is the deliberate relaxation of the muscles of the pelvic floor which precipitates the reflexes of micturition, and the willful contraction of these muscles which cause cessation of the stream. The descent of the bladder base, in consequence of the relaxation of these large, striated muscles and the sharp ascent of the bladder base when these muscles are deliberately contracted, can be readily seen on the fluoroscopic screen by anyone. Our study, which has demonstrated the distinct voluntary mechanism, does not brush aside everything else which has been learned about bladder physiology by cystometry or animal experimentation.

The second point we wish to emphasize is that abolition of the voluntary mechanism, either by fixation of the bladder base, as in advanced cancer of the prostate, or by flaccid paralysis of the pelvic floor muscles, makes it impossible for man to start or to stop micturition at will, and urination thus becomes entirely automatic; i.e., the bladder contents are expelled spontaneously when the bladder has filled to the point of critical stretch. The symptoms of a "cord bladder" therefore are not so much dependent on the specific nerve lesion with which it is associated, but rather do they depend on the status of the bladder, whether overstretched or of normal capacity, on the degree of the urethral resistance to the outflow of urine, and on the condition of the voluntary mechanism, i.e., the muscles of the pelvic floor.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

TRANSURETHRAL RESECTION FOR NEUROGENIC VESICAL DYSFUNCTION IN CASES OF DIABETIC NEUROPATHY

JOHN L. EMMETT
Section on Urology, Mayo Clinic
RICHARD V. DAUT
Fellow in Urology, Mayo Foundation,
AND
RANDALL G. SPRAGUE
Division of Medicine, Mayo Clinic, Rochester, Minnesota

It is now more than 80 years since it was first observed that a characteristic type of nerve disorder occurs as a complicating factor in some cases of diabetes mellitus. Among these early observations was that of a type of vesical dysfunction or paralysis that seemed to be one of the neurologic manifestations of diabetes in some cases. During the past two decades considerable interest concerning this problem has been stimulated by the studies of several investigators, among whom may be mentioned Woltman and Wilder in 1929, Jordan and Crabtree in 1935, Rudy and Muellner in 1941 and Rundles in 1945.

A brief general statement of the clinical manifestations of diabetic neuropathy[1] is found in the summary of the article by Woltman and Wilder. They stated: "Diabetic neuritis is mainly a sensory disturbance without corresponding motor impairment; pain, paresthesia and areflexia are its main characteristics. It shows also a marked predilection for the lower extremities."

By virtue of the fact that the disease involves chiefly the sensory side of the nervous system, motor disturbances as a rule are not conspicuous. The most common finding on neurologic examination is diminution or absence of the tendon reflexes in the lower extremities. Rundles found that the Achilles reflexes were absent in 81 per cent of his 125 patients with diabetic neuropathy. In 56 per cent of the same group the patellar reflexes were absent on one or both sides. Other common findings are diminution or absence of the vibratory sense at the ankles, areas of diminished or absent cutaneous sensibility to touch and extreme muscle tenderness, especially of the muscles of the calf. The patient experiences severe pain which may be dull and aching or which may simulate the darting or lightning pains of tabes. Argyll Robertson pupils (fixed to light but reacting normally in accommodation) occasionally are present. Vesical dysfunction of varying degree may accompany the clinical syndrome.

The clinical picture suggests that the lesion involves principally the sensory portions of the peripheral nerves, the posterior roots and possibly also the posterior columns of the spinal cord. In some instances, particularly if Argyll Robertson pupils and vesical dysfunction are present, there may be considerable difficulty in distinguishing the disorder from true tabes dorsalis of syphilitic origin. Because of the similarity of the two conditions, the term "diabetic tabes" (pseudotabes diabetica) has been coined. Tenderness of the muscles of the calf in diabetic tabes often serves to distinguish it from syphilitic tabes dorsalis. Ordinarily, there is little difficulty distinguishing diabetic neuropathy from other forms of true neuritis. To quote again from Woltman and Wilder: "Striking clinical dissimilarity between neuritis of diabetes and that produced by alcohol, lead, diphtheria and other common causes of neuritis is the almost exclusive predilection in the diabetic neuritis for sensory disturbances."

---

[1] The term "diabetic neuropathy" is now considered to be preferable to the older designation "diabetic neuritis," since the condition in most instances is probably not a true inflammatory disease of the peripheral nerves.

In diabetic neuropathy the total protein content of the cerebrospinal fluid is frequently increased beyond the normal maximum of 40 mg. per 100 cc. It exceeded this value in 24 of 41 cases studied by Swartz at the Mayo Clinic, the values ranging from 45 to 180 mg. per 100 cc.

Clinical observations support the view that the visceral sensory nerve fibers which are components of the sensory portions of the peripheral nerves and the posterior roots may also be involved in the pathologic process. Evidence which favors this hypothesis includes such facts as deficiencies in sweating and loss of vasomotor and pilomotor control, dependent edema and vesical dysfunction or "paralysis." As will be shown later, the type of vesical dysfunction is almost identical with that found in patients with true tabes dorsalis.

PATHOLOGY OF DIABETIC NEUROPATHY

Unfortunately, pathologic studies of necropsy material in cases of diabetic neuropathy are meager. In 1929 Woltman and Wilder found reports of only 42 cases in the literature in which gross or microscopic examination of all or parts of the nervous system had been made in patients with diabetic neuropathy who came to necropsy. They summarized the findings in these 42 cases as follows: Evidence of degeneration of the funiculi of the cord, chiefly in the posterior column, was present in 16 cases; degeneration of the intramedullary portion of the posterior roots in 4 cases; variable changes in the anterior horns in 8 cases; and degeneration in the peripheral nerves in 24 cases. A number of these reports were based on observations that were made before modern neuropathologic techniques became available and it may be questioned whether all of the lesions that were described were related to the diabetes that had been present. They also reported 10 cases of their own in which gross and microscopic examination of the nervous system had been done; in 4 of these cases the examination was made at necropsy. In 3 cases the spinal cord and peripheral nerves had been examined, while in 1, only the peripheral nerves were studied. In the remaining 6, examination was made of the peripheral nerves in legs which had been amputated because of diabetic gangrene. The results of their study showed that there was extensive degeneration of the peripheral nerves in 8 cases and less marked degeneration in 2. "It was usually diffuse, but in 2 cases it was patchy and involved isolated bundles of fibres lying in the midst of relatively normal bundles." They also noted thickening in the walls of the intraneural vessels which made them postulate that some of the involvement of the nerves may be on the basis of arteriosclerosis. The findings in the 3 spinal cords examined were rather disappointing, as there was only slight degeneration seen, which could have been explained on the basis of senility and arteriosclerosis.

Since this study was made, a few isolated reports have appeared from time to time, but no extensive pathologic study of the nervous system in diabetes has appeared. Gill in 1936 reported a case of diabetic neuropathy with cord bladder in which postmortem examination of the spinal cord showed "unmistakable evidence of degeneration of the cord and posterior nerve roots of a non-inflammatory nature. The most striking changes were in the columns of Burdach and Goll and in the posterior roots."

Root and Rogers described a patient of Dr. Hyman Morrison. The patient had diabetic neuropathy and died of pneumonia. On postmortem examination of the cord, the most striking change was the presence of numerous small corpora amylacea. These were most numerous in the dorsal part of the cord and were found not only in the white and gray matter, but also in the overlying meninges. There was a slight diffuse gliosis of the dorsal columns, but no large areas in which the nerve fibers were deficient were found anywhere. This change was found both in the lumbar and thoracic portions of the cord.

Sheppe in 1936 found changes in the posterior roots and posterior columns but also noted changes in the lateral columns and anterior horns. He reported on 5 patients with diabetic neuropathy, 2 of whom suffered from diabetic neurogenic bladder. Both of these latter patients died as a result of urinary infection. In 1 case, that of a man 49 years of age, examination of the spinal cord was made at necropsy. Sheppe summarized his findings as follows: "I feel that it is safe to say that advanced degrees of diabetic neuropathy are represented by degeneration of fibres in the dorsal and lateral columns and anterior horns of the spinal cord, marked degeneration of the nerve roots and extensive demyelinization of the peripheral nerve fibres."

Jordan, Randall and Bloor emphasized the susceptibility of the myelin sheath to degeneration in diabetic neuropathy.

INCIDENCE AND ETIOLOGY OF DIABETIC NEUROPATHY

It is difficult to estimate the incidence of neuropathy in diabetic patients. Rundles found 125 patients with diabetic neuropathy among approximately 3,000 diabetic patients, a rate of approximately 4 per cent. At the clinic year after year the diagnosis of diabetic neuropathy is recorded in approximately 4 to 5 per cent of all cases of diabetes.

The cause of diabetic neuropathy is still obscure. It occurs most commonly in diabetes of relatively long duration and is frequently associated with other "degenerative" complications of diabetes, such as retinopathy and intercapillary glomerulosclerosis. It is even difficult accurately to ascribe diabetic neuropathy to any other definite contributing factors except that many physicians feel that it occurs more often in patients in whom glycosuria has been poorly controlled for long periods. There is general agreement that the degree of severity of the diabetes is not closely correlated with the incidence of diabetic neuropathy. The actual agent that attacks the nerve tissue is not known. Probably different factors play a predominant etiologic role in different cases. For example, in some instances in which the patient has arteriosclerosis obliterans the neuropathy is almost certainly due chiefly to ischemia of the peripheral nerves. In other instances in which evidence of ischemia has been minimal or lacking, the neuropathy has been attributed, rightly or wrongly, to a variety of factors. Possibly the presence of diabetes renders the nerve tissue more vulnerable to a number of different noxious agents.

VESICAL DYSFUNCTION ASSOCIATED WITH DIABETIC NEUROPATHY

The earliest investigators of diabetic neuropathy recognized that disturbances in micturition and "bladder paralysis" were occasionally part of the clinical picture in this disorder. This complication, however, has been considered rather rare until the last 10 or 15 years, during which more frequent reports of cases of this type have appeared. Among those who have reported cases of "diabetic cord bladder" may be mentioned McKittrick and Root in 1928, Jordan and Crabtree in 1935, Gill in 1936, Jordan in 1936, Sheppe in 1936, McLellan in 1939, Rudy and Muellner in 1941 and Rundles in 1945.

The vesical dysfunction is characterized primarily by urinary retention associated with a distended atonic bladder. It simulates closely the condition seen in true tabes dorsalis. It is usually insidious in onset and development, so that it may not be recognized until a palpable tumor of the lower part of the abdomen demands investigation or until nocturnal incontinence heralds a distended bladder with overflow. A careful history in such cases may elicit the story, so common in true tabetic patients, of a gradual increase in the interval between voidings until micturition has been necessary only once or twice daily. Patients also offer the information that considerable straining may be necessary to evacuate the bladder. Less frequently, patients may complain of some diurnal incontinence which has been spoken of in the literature as "disturbances of the sphincters."

In other patients the urinary symptoms more nearly simulate those found in ordinary prostatic obstruction such as frequency, nocturia, poor dribbling stream and a feeling of incomplete emptying of the bladder. In some patients the retention comes on suddenly as a result of some acute complicating illness or after a surgical operation.

Cystoscopic examination usually reveals a large atonic bladder with minimal to moderate trabeculation and a large quantity of residual urine, which is frequently infected. In young individuals the vesical neck may appear almost normal, whereas in older male patients (in the age at which prostatism occurs) there may be associated prostatic hyperplasia. Investigators who have studied the vesical dysfunction with cystometrograms are quite generally agreed that the condition should be classified as atonic neurogenic bladder.

It is difficult to estimate the incidence of this complication in diabetes, as it is not always possible to distinguish clearly between simple prostatic obstruction in a case in which diabetes or diabetic neuropathy is only a coincidental finding and a true atonic neurogenic bladder resulting from diabetic neuropathy. This same problem in differential diagnosis occurs in patients with tabes dorsalis and has been discussed fully elsewhere by Beare and one of us. Some idea of the frequency of diabetic neurogenic bladder may be had from the study of Rundles. Of the 125 cases of diabetic neuropathy which he encountered in a group of almost 3,000 diabetics, 18 were found to have "an atonic type of bladder paralysis." He also stated that 10 patients complained of some type of urinary incontinence.

Up to the present time, the treatment of diabetic neurogenic bladder has been conservative and, for the most part, rather unsatisfactory. It has consisted mainly of control of the diabetes, adequate diet, vitamins, administration of urinary antiseptics and teaching the patient to void at regular intervals, employing abdominal straining and manual compression (Credé) where necessary. That part of the treatment which has been aimed at the control of the underlying diabetic neuropathy has been particularly ineffective. In patients with more advanced disease and in those not responding to conservative measures, drainage has been instituted by means of intermittent or indwelling urethral catheter or suprapubic cystostomy. The results of treatment have not been too encouraging and many patients succumb to infection. Jordan and Crabtree summarized their experience with 7 patients as follows: "The prognosis is not good. Three of the 7 patients are dead. None of our patients has regained the power to empty the bladder completely. The blood nitrogen, on the other hand, has not risen to a serious level and the general health of the patients has remained reasonably good."

Rundles was a little more optimistic in his evaluation of conservative treatment. Although recognizing that most patients are unable to empty the bladder completely, he wrote: "If recognized early and treated well the condition may remain entirely benign." Rudy and Muellner emphasized the lethal possibilities of urinary infection in diabetics and advised against instrumentation and the use of catheters whenever possible. In 4 of the 11 cases they reported, death occurred, 2 of which resulted from severe urinary infection. They felt that "the prognosis, contrary to the general belief, is fair in properly treated cases."

TRANSURETHRAL RESECTION IN THE MANAGEMENT OF DIABETIC NEUROGENIC BLADDER

It seems obvious from the foregoing discussion that the vesical dysfunction found in patients with diabetic neuropathy is essentially the same as that encountered in patients with true tabes dorsalis. It assumes greater importance in the diabetic patient, however, because of the greater potential danger of infection. Infected residual urine in a diabetic patient may easily precipitate a lethal infection of the genito-urinary tract. For this reason adequate treatment is important.

It must be emphasized that all cases of urinary retention in diabetic patients either with or without associated neuropathy are not cases of atonic cord bladder. The majority of patients past 50 years of age no doubt have simple obstruction of the vesical neck with urinary retention, and diabetes mellitus is only a coincidental finding. It is apparent that the diagnosis of diabetic neurogenic bladder in young people should not be difficult, as the incidence of obstruction of the vesical neck in the first three decades of life is low. In older male patients the difficulty of accurate differential diagnosis increases because of the probability of prostatic hyperplasia. In some patients in this age group, both neurogenic vesical dysfunction and prostatic obstruction may be present. In some cases accurate differentiation may not be possible, but this is not important because the treatment in either case is the same. The problem involved is so similar to that of the atonic neurogenic bladder of the patient with true tabes dorsalis that we are quoting below an explanation of the problem by Emmett and Beare. The explanation of the mechanics involved in the vesical dysfunction of patients with tabes dorsalis applies equally well to the patients with diabetic neuropathy.

"In making such a study, it must be emphasized that it is impossible in every case to distinguish accurately vesical dysfunction caused by the tabetic state alone from that which results from hypertrophy of the prostate gland or other obstruction of the vesical neck in a case in which tabes dorsalis is only a coincidental finding and of no urologic importance. It is true that the extremes of these conditions are quite easily recognized, but intermediate conditions may be difficult to classify. The chief reason for this difficulty lies in the basic neuromechanics and obstructive factors involved in the disability. The neurophysiology of normal micturition has been described elsewhere, and it is so well known that description here seems unnecessary. The tabetic process damages the posterior spinal ganglia, the posterior sensory roots and the posterior sensory columns of the spinal cord. This may block not only the impulses which pass through the sensory component of the simple spinal reflex arc and which control micturition (the level of which is in the sacral portion of the cord) but also may block the impulses which pass through the sensory part of the suprasegmental conditioning reflex and mediate vesical control by means of subconscious or conscious inhibitory impulses from the higher levels. With involvement of the sensory component of the lower reflex arc, it is apparent that more and stronger impulses would be necessary to incite reflex vesical contraction. This would result in progressive vesical distention, loss of tone, and atony. Damage to the sensory component of the suprasegmental conditioning reflex would interfere with the stimuli which incite the proper flow of inhibitory impulses down the corticospinal tracts to supply subconscious and voluntary control of the lower reflex arc for micturition. In other words, the patient might not experience the desire to micturate until greater and greater distention of the bladder occurs, and the micturition could begin without the patient being aware of it.

"It is easy to visualize how such a lesion can give rise to urinary retention and incontinence. The bladder becomes increasingly stretched, loses its tone and becomes atonic. There results an imbalance between the detrusor urinae muscle and the vesical neck, which results in residual urine and retention. Under such circumstances, even a normally appearing vesical neck may be obstructive. Any obstruction of the vesical neck, even of a minimal degree, may increase the imbalance. . . .

"Our experience with this problem has left us with the impression that most of the urinary incontinence in tabetic patients may be explained in two ways: 1) overflow from a distended bladder, and 2) involuntary micturition caused by reflex emptying of the bladder not properly controlled by the suprasegmental conditioning reflex, the sensory components of which have been damaged. To put it simply, since the patient is not aware that micturition is about to occur, sufficient inhibitory impulses are not sent down from the conscious or subconscious level to prevent it.

"It is apparent, therefore, that the over-all problem of vesical dysfunction in tabetic patients is composed of three rather ill-defined parts; namely, 1) vesical dysfunction arising primarily from the neurogenic lesion caused by the tabetic state, 2) obstruction of the vesical neck in a case in which tabes dorsalis is only a coincidental finding and plays no part in the vesical dysfunction and 3) a combination of both factors."

It should be apparent to the reader that if in the last paragraph in the preceding quotation the terms "diabetic" and "diabetes" be substituted for "tabetic" and "tabes dorsalis," the problem of vesical dysfunction in the diabetic is accurately stated.

Inasmuch as the results of transurethral resection of the vesical neck in patients with tabetic cord bladder have been so favorable, we have felt that equally good results should be possible in patients with diabetic neurogenic bladder who have not responded to conservative treatment. Inasmuch as we safely do many transurethral prostatic resections each year at the clinic for prostatic enlargement in patients with diabetes, it seemed to us that the hazard of such a procedure in a patient with a diabetic neurogenic bladder should be of less magnitude than the constant presence of infected residual urine or the trauma incident to intermittent or permanent urinary drainage by means of urethral catheter or suprapubic cystostomy. Our thesis is supported, we believe, by 3 cases of diabetic neurogenic bladder in which successful treatment was carried out by means of transurethral resection of the vesical neck.

Case 1.—A man 32 years of age was admitted to the clinic on May 3, 1942. His presenting complaint was "inability to urinate." He stated that 12 years previously, in 1930, he had been found to have diabetes mellitus, and he had been treated with insulin. In 1934, as a consequence of neglect of treatment, diabetic coma had developed. Recently, he had been taking 30 units of protamine zinc insulin daily in the evening before supper. No systematic diet had been followed.

For approximately 6 years he had been having diarrhea which was characterized by frequent loose, copious stools, sometimes containing undigested food. The diarrhea had been particularly troublesome at night and had sometimes been associated with fecal incontinence. Two years before admittance he had noticed a mild orthostatic edema of the feet and ankles. In the past few weeks this had become worse and had extended to the legs, thighs and buttocks. For approximately a year he had experienced numbness of the feet and legs. This had been associated with impaired sensation, manifested by an inability to recognize the temperature of his bath water. There had been no motor disturbances.

The patient stated that for the past year he could not remember having felt any desire to urinate. About 2 months before admittance he had noted some slowing of the urinary stream and slight nocturnal incontinence of urine. Because of some suprapubic fullness, his home physician had catheterized the bladder and found 3,000 cc of residual urine to be present. Since then he had been catheterized once daily.

On physical examination the principal findings were evidences of undernutrition, a rounded suprapubic mass extending almost to the umbilicus and slight edema of the ankles. The blood pressure was 138 systolic and 95 diastolic, expressed in millimeters of mercury. Examination of the ocular fundi revealed an extensive diabetic retinopathy and minimal sclerosis of the retinal arterioles.

Neurologic examination disclosed marked diminution in the tendon reflexes of the upper and lower extremities. There was some loss of pain, temperature and vibratory sense in the legs, but there was no well-defined level. The muscles of the calves were tender. The Romberg sign was present. The pupils reacted feebly to light and accommodation. The value for total protein in the spinal fluid was 40 mg. per 100 cc, the results of serologic tests for syphilis were negative and the colloidal gold curve was normal. A neurologic diagnosis of diabetic pseudotabes was made.

After a detailed investigation of the gastro-intestinal tract, a diagnosis of so-called diabetic diarrhea and possible chronic pancreatitis was made. The edema of the lower extremities proved to be related to hypoproteinemia.

Urologic examination showed the bladder to be distended almost to the umbilicus. An indwelling catheter was inserted and 1,500 cc of urine which contained microscopic pus and blood were obtained. A cystometrogram revealed a markedly atonic bladder with no emptying contractions. Cystoscopy revealed a large atonic bladder with poor expulsive force. There seemed to be a definite contractile ring around the vesical neck. The bladder was moderately trabeculated.

After the diabetes had been brought under control, transurethral resection of the vesical neck was carried out on May 22, 1942. Five grams of tissue were removed from the entire circumference of the vesical neck and prostatic urethra. The tissue was examined microscopically and reported to show "hyperplasia of muscle and inflammatory tissue."

After operation the patient was able to void easily, but a residual urine amounting to approximately 200 cc persisted.[2] Accordingly, the patient was allowed to return home and was advised to have his bladder lavaged occasionally.

During the succeeding 3 years the patient continued to void without difficulty. The residual urine on numerous occasions varied between 25 and 600 cc, but for the most part approximated 200 cc. The diarrhea persisted and there was gradual deterioration in his general condition. He died at home on December 27, 1945, from the combined effects of malnutrition and a pulmonary infection of unknown origin.

[2] This patient was operated upon early in the course of our experience with the treatment of cord bladder by transurethral resection of the vesical neck. At that time we were not aware of the fact that in many such cases a second or even third resection is necessary to restore normal vesical function.

Case 2.[3]—A man aged 31 years was admitted to the clinic on September 15, 1944. He stated that he had first become ill in 1937 with symptoms of polydipsia, polyuria and polyphagia. He stated that he had been treated by a chiropractor but that a diagnosis of diabetes mellitus was not established until 1940, when he consulted a physician because of persistence of the same symptoms. He was given a diet and instructed to take 20 units of soluble insulin 2 times daily. No systematic dietary regimen had been followed. He had not examined his urine for the past year. His principal complaints upon admission were general malaise, polydipsia, polyuria, backache, diarrhea and loss of weight.

The results of general physical examination were negative except for evidences of undernutrition and a traumatic perforation of the nasal septum. Examination of the ocular fundi revealed many small punctate hemorrhages and conglomerate white punctate exudates around the macular regions of both eyes, typical of diabetic retinopathy. A single specimen of urine contained 10.91 gm. of glucose (4.85 per cent) and the value for fasting blood sugar was 426 mg. per 100 cc. The blood urea measured 30 mg. per 100 cc. Urinalysis showed marked pyuria, although the patient complained of no urinary symptoms except polyuria. An excretory urogram showed normal kidneys but the vesical outline was large.

Results of other laboratory and special tests, including determination of hemoglobin, erythrocyte count, leukocyte count, differential count, flocculation test for syphilis, roentgenographic examination of the thorax and lumbar part of the spinal column, stool examinations, proctoscopic examination, and roentgenoscopic examination of the colon and terminal part of the ileum, the stomach and the duodenum, were negative or normal. A diagnosis was made of diabetes mellitus, grade 4, diabetic retinopathy, "diabetic diarrhea" and urinary infection. The diabetes was brought under control with the aid of a mixed dose of protamine zinc and regular insulin totaling 84 units daily. The pyuria was eliminated with the aid of sulfathiazole.

The patient returned to the clinic about 3 months later (December 29, 1944). He stated that he had got along well for 1 month after dismissal from the clinic and then had come down with the "flu" which was characterized by the occurrence of chills, fever, malaise and generalized aching. Shortly thereafter he noticed difficulty passing urine and began to experience stabbing pains over most of the body, but most marked in the legs and left groin. The diarrhea had persisted.

Neurologic examination revealed areas of marked hyperesthesia over both thighs anteriorly in the part supplied by the femoral cutaneous nerves. The knee and ankle jerks were absent. There was exquisite tenderness of the quadriceps and calf muscles. The pupils reacted normally to light and accommodation. Results of examination of the spinal fluid were negative except for a total protein content of 75 mg. per 100 cc.

Urologic examination showed the urine to be moderately infected with Streptococcus faecalis. Several determinations of residual urine gave values which varied from 400 to 700 cc. Cystoscopy revealed a large atonic bladder with minimal trabeculation and moderate cystitis. The vesical neck did not appear to be especially obstructive. The patient was treated conservatively with urinary antiseptics and intermittent vesical lavage. The urinary retention persisted but the patient was allowed to return home in the hope that the vesical function might improve if there was improvement in the symptoms of diabetic neuropathy. To this end, treatment with crude liver extract, vitamin supplements and careful management of the diabetes was advised.

---

[3] This case was referred to by Emmett and Dunn.

The patient returned 4 months later (April 13, 1945). There had been some improvement in the pains in his legs, but he complained of burning paresthesia in the thighs. His diabetes had remained reasonably well controlled with the dosage of insulin previously prescribed. The urinary difficulty persisted. Several examinations showed 200 to 300 cc of infected residual urine. Cystoscopic examination gave essentially the same results as at his previous visit. The patient was treated by means of an indwelling urethral catheter and urinary antiseptics. This treatment did not improve vesical function, however, and the symptoms of poor, interrupted stream and residual urine persisted.

Transurethral resection was done on April 30, 1945. With the knife punch, 5 gm. of tissue were removed, although the vesical neck did not appear especially obstructive before the operation was started. Microscopic examination of the tissue removed showed adenofibromatous hyperplasia of the prostate gland. The urethral catheter was removed on the third postoperative day but the patient did not void well. Therefore, on the fifth postoperative day a second stage transurethral resection was performed. The resection was carried more deeply at the vesical neck, removing an additional 3 gm. of tissue. When the catheter was removed the patient voided easily, producing a forceful stream of normal size. The first postoperative check of residual urine showed 250 cc to be present but after a few days the amount had decreased to 100 cc. There was no frequency or nocturia and the patient was allowed to return home.

Six weeks after dismissal the patient wrote that he was still voiding normally and that examination showed less than 30 cc residual urine to be present. At that time he was still experiencing symptoms attributable to diabetic neuropathy.

The patient returned in July 1946, approximately 15 months after operation, because of failing vision. Examination of the ocular fundi revealed that the diabetic retinopathy had progressed markedly. The diabetes had been controlled fairly well with the aid of a mixed dose of protamine zinc and regular insulin totaling 68 units a day. Symptoms attributable to diabetic neuropathy had virtually disappeared although tenderness of the calves and diminution of the tendon reflexes in the lower extremities persisted. His diarrhea had largely subsided. The presence of albuminuria, retinopathy and mild renal insufficiency suggested that he might have the lesions of intercapillary glomerulosclerosis. There were no urinary symptoms. Vesical function was normal. There was no residual urine, and the urine gave negative results on microscopic examination.

Case 3.—A man aged 26 was first admitted to the clinic on December 11,

1944. His presenting complaint was diarrhea of 18 months' duration. He stated that a diagnosis of diabetes had been made several years previously. This had apparently been adequately controlled by means of diet and insulin. He was taking 50 units of protamine zinc insulin each morning and 12 to 20 units of regular insulin each evening.

The results of physical examination were essentially negative except for infected tonsils. A cursory neurologic examination gave negative results except for hypo-active tendon reflexes in the lower extremities. Roentgenoscopic examination of the colon and terminal portion of the ileum gave negative results. Proctoscopic examination for a distance of 24 cm. gave normal results. Urinalysis revealed a slight reduction of Benedict's solution, and albuminuria, grade 2 (on a basis of 1 to 4, 1 representing the mildest and 4 the most severe condition). The results of microscopic examination of the urine were negative. The value for fasting blood sugar was 166 mg. per 100 cc. The results of other laboratory studies, including determination of the hemoglobin, erythrocyte count, leukocyte count, differential count, flocculation test for syphilis, gastric analysis and roentgenographic examination of the thorax were negative or normal. The diarrhea was treated empirically, with slight improvement, and the patient was dismissed.

The second admission to the clinic was on October 11, 1947. At that time the patient was obviously sick and had numerous complaints. He stated that the diarrhea had persisted since his previous visit, and on occasions he had experienced fecal incontinence at night. Also, for about 3 years he had experienced at intervals a sensation of "pins and needles" in the lower extremities which had been constant for the past 2 weeks. This was associated with cramps and soreness in the muscles of his legs. For the past 3 or 4 years troublesome urinary symptoms had developed gradually and increased in severity. These consisted of diurnal frequency, nocturnal frequency characterized by urination every half hour, and some "incontinence" especially when he was asleep. The urinary stream was poor and associated with some urgency and burning. About the same time that the urinary symptoms had become prominent the patient had experienced a gradual decrease in libido so that for the past few months he had considered himself impotent. Two weeks prior to admittance the patient had experienced an attack of chills and fever. Pyuria had been discovered, for which sulfonamides had been prescribed. Recently there had been some edema of the ankles and dyspnea on exertion. He had been taking 40 units of protamine zinc insulin each morning and had been experiencing occasional insulin reactions in the early morning hours.

On physical examination the blood pressure was found to be 120 systolic and 70 diastolic. The patient was moderately undernourished. There was a mass in the lower part of the abdomen. Urethral catheterization disclosed the mass to be a distended bladder from which 700 cc of cloudy urine were withdrawn. A urethral catheter was left in place for drainage. Neurologic examination disclosed moderate diminution in touch, pain, vibratory and joint sense of the lower extremities. The muscles of the calves were tender and the tendon reflexes of the lower extremities were absent, even with reinforcement. Examination of the ocular fundi disclosed no evidence of diabetic retinopathy.

Laboratory examinations gave the following results: albuminuria, grade 3; melituria, grade 4; and pyuria, grade 4. The value for fasting blood sugar was 238 mg. per 100 cc. The value for hemoglobin and the erythrocyte count were normal. The leukocyte count was 20,200 per cubic millimeter of blood. Special smears of the blood revealed polymorphonuclear leukocytosis. The results of roentgenographic examination of the heart and lungs were negative. Examination of the spinal fluid gave negative results except for a total protein content of 60 mg. per 100 cc. Results of examination of the urine for abnormal porphyrins, lead and arsenic were negative. Parasites and ova were not found in several stool specimens. The fat content of the stools was 36.2 and 46.7 per cent (dry weight) on two occasions.

The consulting neurologist made a diagnosis of diabetic myeloneuropathy.

Further urologic investigation gave the following results. Roentgenograms of the kidneys, ureters and bladder and an excretory urogram revealed a small stone in the tip of one of the calyces of an otherwise normal-appearing right kidney. The left kidney was urographically normal. Culture of urine from the bladder showed Escherichia coli and Streptococcus faecalis.

The patient was kept under observation and medical management in the hospital for 5 days. Glycosuria was reasonably well, though not entirely, controlled with the aid of a mixed dose of protamine zinc and regular insulin totaling 44 units a day, and a diet containing 187 gm. of carbohydrate, 90 gm. of protein and 170 gm. of fat. Diarrhea was only slightly relieved by symptomatic treatment and it was felt that this represented a so-called diabetic diarrhea. The urethral catheter was removed several times but residual urine amounting to about 500 cc persisted.

On October 18, 1947, transurethral resection of the vesical neck was done with the patient under pentothal sodium anesthesia. The bladder showed trabeculation, grade 2, and it was spastic.[4] In spite of the previous excessive retention it was impossible to introduce more than 2 or 3 ounces (60 to 90 cc) of irrigating fluid into the bladder. Four grams of tissue were removed from the entire circumference of the vesical neck with the small cold knife punch. The tissue was examined microscopically and reported to be "inflammatory muscle." There was no postoperative fever. The catheter was removed on the seventh postoperative day. The patient voided poorly and residual urine amounting to 150 to 375 cc persisted.

On the eleventh postoperative day a second-stage transurethral resection was done with the patient under pentothal sodium anesthesia. At this operation the bladder was relaxed so that the resection could be done more easily than at the previous sitting. An additional 4 gm. of tissue were removed, the resection being carried rather deeply at the vesical neck and an attempt being made to remove all prostatic tissue out to the verumontanum. This tissue was examined microscopically and called "inflammatory muscle." The result of this procedure was good. When the catheter was removed on the fourth postoperative day, the patient voided normally with good control and emptied his bladder completely. When the patient was dismissed to return home on November 7, his urinary function was entirely normal aside from the fact that he had to urinate once at night. He was emptying the bladder completely at each micturition. There was no subjective or objective change in the neurologic disturbances in the lower extremities. Glycosuria was well controlled with the aid of 8 units of protamine zinc and 24 units of regular insulin taken as a mixture in one syringe in the morning before breakfast.

---

[4] It is difficult to explain this phenomenon of spasticity in an atonic bladder which had been carrying more than 500 cc of residual urine. This unusual situation, however, is occasionally observed in patients with simple prostatic obstruction unassociated with a neurologic lesion in whom there has been excessive urinary retention. We have felt at times that the anesthetic agent might be a factor, although we have observed the phenomenon with spinal and sacral block as well as with intravenous pentothal sodium anesthesia.

The patient returned on December 17, 1947, because of fever, malaise and backache during the previous 3 weeks. He had been voiding normally and emptying his bladder completely. He had been treated with penicillin and streptomycin, which seemed to control the fever, but as soon as administration of the medicine was discontinued the fever would recur.

Examination revealed moderate tenderness and muscle spasm in the right lumbar region. Urinalysis revealed pyuria, grade 2, with 50 cells per high-power field. The value for blood urea was 38 mg. per 100 cc. There was no residual urine. On cystoscopic examination the bladder appeared normal and the prostatic urethra was well healed. Bilateral pyelograms revealed incomplete filling of the upper calyx of the right kidney, suggestive of extracalyceal pressure. The left kidney was normal. A diagnosis of cortical abscess of the right kidney was made.

The right kidney was explored surgically on December 20, 1947. Multiple abscesses were found in the upper half of the kidney. Nephrectomy was performed. Following the operation there was a gradual rise in the value for the blood urea, which stabilized at about 78 mg. per 100 cc. The patient was free of fever and his general condition was much improved. His diabetes was well controlled with the aid of a mixture of 6 units of protamine zinc and 14 units of regular insulin taken in the morning before breakfast. At the time of dismissal on January 16, 1948, he was voiding normally and there was no residual urine. He was instructed to maintain a high fluid intake and to have a determination of the blood urea in 1 month.

SUMMARY

The treatment, by transurethral resection of the vesical neck, of 3 patients who had neurogenic vesical dysfunction associated with diabetes mellitus and diabetic neuropathy is reported. The atonic type of vesical dysfunction observed in these cases closely simulated that which is seen in association with tabes dorsalis of syphilitic origin. In 1 case transurethral resection of the vesical neck resulted in moderate improvement in vesical function; in this case the amount of tissue resected was not adequate for an optimal result. In the other 2 cases resection of the vesical neck resulted in restoration of essentially normal micturition. In the absence of effective methods of therapy of the diabetic neuropathy which is responsible for the vesical dysfunction in these cases, resection of the vesical neck provides a means of improving vesical function and thereby protecting the patient against the inconvenience and hazards involved in carrying infected residual urine in the bladder.

REFERENCES[5]

BONARDI, E.: Sclerosi diffusa pseudo-sistematizzata del midolla spinale con polinevrite in un case di diabete mellito. Morgagni, 39: 557–564, 1897.

BRAASCH, W. F. AND THOMPSON, G. J.: Treatment of atonic bladder. Surg., Gynec. & Obst., 61: 379–384, 1935.

DE CALVI, MARCHAL: Quoted by Jordan, W. R. and Crabtree, H. H.

DEES, J. E. AND LANGWORTHY, O. R.: An experimental study of bladder disturbances analogous to those of tabes dorsalis. J. Urol., 34: 359–371, 1935.

EMMETT, J. L.: Urinary retention from imbalance of detrusor and vesical neck; treatment of transurethral resection. J. Urol., 43: 692–704, 1940.

EMMETT. J. L. AND BEARE, J. B.: Bladder difficulties of tabetic patients with special reference to treatment by transurethral resection. J. A. M. A., 117: 1930–1934, 1934.

EMMETT, J. L. AND BEARE, J. B.: Transurethral resection for vesical dysfunction in cases of tabes dorsalis. J. A. M. A. 136: 1093–1096, 1948.

EMMETT, J. L. AND DUNN, J. H.: Transurethral resection in the surgical management of cord bladder. Surg., Gynec. & Obst., 83: 597–612, 1946.

FEIN, H. D., RALLI, ELAINE P. AND JOLLIFFE, NORMAN: Peripheral neuropathy due to vitamin B_1 deficiency in diabetes mellitus. J. A. M. A., 115: 1973–1976, 1940.

GILL, R. D.: The diabetic (cord) bladder, J. Urol., 36: 730–739, 1936.

JORDAN, W. R.: Neuritic manifestations in diabetes mellitus. Arch. Int. Med., 57: 307–366, 1936.

JORDAN, W. R. AND CRABTREE, H. H.: Paralysis of the bladder in diabetic patients. Arch. Int. Med., 55: 17–25, 1935.

JORDAN, W. R., RANDALL, L. O. AND BLOOR, W. R.: Neuropathy in diabetes mellitus; lipid constituents of the nerves correlated with the clinical data. Arch. Int. Med., 55: 26–41, 1935.

MCKITTRICK, L. S. AND ROOT, H. F.: Diabetic surgery. Philadelphia: Lea & Febiger, 1928, p. 253.

MCLELLAN, F. C.: The neurogenic bladder. Springfield, Ill. Charles C Thomas, 1939, p. 172.

NESBIT, R. M. AND GORDON, W. G.: Neurogenic bladder. Pennsylvania M. J., 43: 1261–1268, 1940.

ROOT, H. F. AND ROGERS, M. H.: Diabetic neuritis with paralysis. New England J. Med., 202: 1049–1053, 1930.

RUDY, ABRAHAM AND MUELLNER, S. R.: The neurogenic bladder in diabetes mellitus: early recognition and treatment with a report of cases. J. Urol., 45: 844–857, 1941.

RUNDLES, R. W.: Diabetic neuropathy; general review with report of 125 cases. Medicine, 24: 111–160, 1945.

SHEPPE, W. M.: Production of pathological changes in nervous system by diabetes mellitus. West Virginia M. J., 32: 9–16, 1936.

SWARTZ, F. C.: Diabetic neuritis. Thesis, Graduate School, University of Minnesota. (May) 1940, 73 pp.

WOLTMAN, H. W. AND WILDER, R. M.: Diabetes mellitus; pathologic changes in the spinal cord and peripheral nerves. Arch. Int. Med., 44: 576–603, 1929.

---

[5] Since [illegible] ation the following article on the subject has [illegible] Grant, Owsley: Vesical abnormalities incident [illegible] 948.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

BACTERIOLOGICAL STUDY OF URINE FROM PARAPLEGIC PATIENTS[1]

SEWARD E. OWEN AND EDMUND P. FINCH

From the Laboratories, Veterans Administration Hospital, Hines, Illinois

The purpose of this study is to provide information on the various types of bacteria found in the urines of paraplegic patients. Of special interest is the variation in bacterial types in the same patients, over the 6 month period covered by this work. The material deals with bacteriologic findings on 274 paraplegic patients.

The literature contains but few reports on the variety of bacterial species found in the urines of paraplegic patients. Petroff and Lucas report 87 cases wherein the bacterial types are limited to 7. They report that urine cultures displayed a mixture of organisms; viz., gram negative bacilli and gram positive cocci and that the former were predominant. Their gram negative group comprised about 92 per cent of the bacterial types found in paraplegic bladders. Keefer et al. in their selection of 409 cases of chronic infections of the urinary tract for streptomycin treatment apparently did not include urinary tract infections in paraplegic patients. Schaub's recent report has considerably clarified the importance of paracolon organisms in urinary tract infections in women. Kennedy, Cummings and Morrow described 22 paracolon strains, 4 of which were isolated from urine. Cross reported a paracolon bacillus in a series of over 20 organisms obtained from urinary tract infections. Levine noted a group of unclassifiable gram negative rods in urinary infections. We have found the paracolon group to be one of major importance in urine from paraplegic patients.

Antibiotic sensitivities vary considerably depending upon natural or acquired resistance. Streptomycin may also change the spreading properties of Proteus; and A. aerogenes colonies may become dry and rugose following streptomycin exposure. Organisms become resistant to streptomycin and it appears fallacious to isolate one colony from a plate, determine its sensitivity, and predict efficiency of future streptomycin therapy on the basis of these findings. Separate colonies of the same type organism from the same plate may show different resistance to the antibiotic. A more exact prediction of organism sensitiveness to streptomycin and its probable efficacy in treatment can only be obtained by fishing several typical colonies to a suspending medium and determining the antibiotic resistence of this mixture.

The coagulase test, which was used routinely on isolated staphylococci in an attempt to classify the virulent strains, in one instance produced unexpected results; viz., 1 case displayed a coagulase positive hemolytic Staphylococcus aureus as well as a coagulase positive similar though nonhemolytic organism.

---

[1] Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

Hemolytic property of the staphylococcus does not thus necessarily parallel coagulase positiveness.

In urinary tract infections commonly encountered, it may be a simple matter to differentiate reinfection from recurrence of primary infection. In paraplegic patients, however, the practical impossibility of properly sterilizing body parts leaves little doubt that the continued use of catheters favors the reintroduction of organisms. This is especially so since the skin areas below the waist of paraplegics are prone to harbor many types of bacteria. Urinary complications are to be expected whenever incompetent sphincters are encountered and when incomplete drainage requires repeated catheterization. It is believed that when bacterial species in cases not receiving antibiotics showed a marked change in sensitivity, that a new infection had occurred in a receptively favorable urinary tract, or that a variant may have developed similar to that noted by Miller and Bohnhoff.

The voluminous data on urine cultures from paraplegic patients accumulating at the laboratories and the many interesting and unusual findings stimulated the preparation of this report. Organisms of 37 different species were isolated in a series of 1882 classifications. The number of urines cultured from each patient varied from 1 to 12. In the early part of the test period the average number of different organisms per urine was 2; later urines displayed an average of 5 different organisms and as many as 7 were noted. This increase is believed to be a result of repeated catheterizations.

One of the many problems encountered in this study was that of isolating all organisms in pure culture for studies of antibiotic sensitivity. Proteus was particularly troublesome, as 52.8 per cent of the cases showed a member of this group. In several instances as many as three Proteus species were found in a single urine culture. The relation of organism occurrence to total number of patients and cultures is shown in table 1. Column 1 shows the number of cases harboring the organism listed. Column 2 gives these data on a percentage basis. The number of times these organisms were encountered in the cultures is presented in column 3, while column 4 gives the percentage incidence of the various organism groups. Since it is difficult to differentiate the etiological organism from secondary invaders, all organisms isolated are listed. The diphtheroids, a common contaminant, were isolated from 23 cases. One diphtheroid displayed hemolysis on blood agar. Yeasts were identified in 5 cases, although no special cultural technique was employed for these. N. catarrhalis, Serrata marcessens, and Klebsiella pneumoniae were reported in 1 instance each. Of the organisms shown in column 4, 75 per cent were gram negative. This figure is considerably lower than that reported by Petroff and Lucas (loc. cit.) for gram negative types found in paraplegic bladders.

Table 2 shows the relative incidence of some of the larger groups of organisms encountered. Proteus, as might be expected, heads the list; 19.2 per cent of all isolations proved to be one of the 6 Proteus species listed. P. vulgaris was nearly twice as common as P. morgani. E. coli were isolated 209 times; hemolysis on blood agar was noticed in 15 instances. This phenomenon probably

TABLE 1. *The relation of organism occurrence to total number of patients and cultures*

ORGANISM GROUP	NUMBER OF CASES SHOWING	PER CENT OF CASES SHOWING	NUMBER OF CULTURES	PER CENT CULTURES SHOWING
Aerogenes	171	62.4	332	17.6
Proteus	143	52.8	361	19.2
Pseudomonas	119	43.4	230	12.2
Escherichia	111	40.5	217	11.5
Enterococci	109	39.8	154	8.2
Paracolon	91	33.2	134	7.1
Achromobacter	86	31.4	120	6.4
Streptococci	84	30.7	157	8.4
Staphylococci	66	24.1	71	3.8
Micrococci	34	12.4	42	2.1
Alcaligenes	25	9.1	26	1.4
Diphtheroids	23	8.4	28	1.5
Yeast	5	1.8	5	0.4
Catarrhalis	2	0.73	2	0.1
S. marcessens	1	0.37	1	0.05
Friedlander	1	0.37	1	0.05

TABLE 2. *Showing the breakdown of some typical bacterial groups*

GENUS	SPECIES	PER CENT OF ALL CULTURES	NUMBER OF CULTURES
Proteus		19.2	
	P. vulgaris		151
	P. morgani		81
	P. rhettgheri		52
	P. mirabilis		51
	P. ammoniae		15
	P. americanus		11
Escherichia		11.5	
	E. coli		194
	E. coli (hemolytic)		15
	E. freundi		8
Streptococci		8.4	
	G. streptococcus		77
	B. streptococcus		41
	A. streptococcus		32
	Other streptococci		7
Enterococci		8.2	
	Strept. fecalis		119
	Other enterococci		35
Staphylococci		3.8	
	S. aureus (hemolytic)		33
	S. aureus (non-hemol.)		12
	S. albus		26

occurred more often but was not considered significant at that time. Of all organisms isolated 11.5 per cent were members of the genus Escherichia. Streptococci were found 157 times or an 8.4 per cent incidence. In 7 early instances unexpected overgrowth resulted; these are listed as "streptococcus others". The later development of Proteus inhibiting agents eliminated the trouble. Staphylococcus albus was found about half as frequently as Staphylococcus aureus. The latter species was subdivided into two groups on the basis of the presence or absence of hemolysis on blood agar. The coagulase test was employed on isolated staphylococcus cultures to differentiate possible pathogenic strains.

The following résumés regarding the bacteriological findings on specimens from paraplegic patients are illustrative of the complexities encountered. PS indicates penicillin sensitivity in units per cubic centimeter; SS indicates sensitivity in units per cubic centimeter of streptomycin. Likewise PR and SR, indicates resistance to these antibiotics in units per cubic centimeter.

CASE SUMMARIES

Case 2. On August 16 the urine showed E. coli SS 7.5; P. ammoniae SS 7.5 B. alcaligenes SS 30; enterococcus SS 7.5; all were sensitive to penicillin at 50 units. On September 13 and 14 blood streptomycin level was 17.4 U/cc and the blood culture was negative. On September 17 culture showed A. aerogenes and P. vulgaris, both resistant to penicillin at 400 U/cc and to streptomycin at 200 U/cc. On October 4 the urine showed A. aerogenes PR 400, P. rhettgeri PS 200; both organisms were resistant to streptomycin at 200 U/cc. On October 22 the urine showed E. coli PS 400, SS 200; Streptococcus fecalis PS 5, SS 25; Achromobacter PS 400 and SS 7.5. This case shows the variation in bacterial flora that may occur spontaneously or following treatment.

Case 19. This case shows a variation in antibiotic sensitivity of Staphylococcus aureus which remained coagulase positive throughout and was hemolytic except on October 2. On August 31 the urine showed S. aureus PR 400, SR 200; beta hemolytic streptococcus PS 0.5, SS 15. On September 16 the urine displayed S. aureus PS 5, SR 200; beta hemolytic streptococcus PS 0.5 and SS 1. On October 2 urine showed S. aureus, nonhemolytic but coagulase and mannite positive, PS 100 and SS 1; pyocyaneus PR 400 and SS 7.5; S. fecalis PS 0.5 and SR 200; S. albus PS 0.5 and SS 7.5; diphtheroid PS 0.5 and SS 1. On October 12 the urine showed S. aureus PR 400 SS 7.5; pyocyaneus PR 400 and SS 15; beta hemolytic streptococcus PS 0.5 and SS 7.5. On October 28 urine culture showed S. aureus PS 100 and SS 200; pyocyaneus PR 400 and SS 50; P. morgani PR 400 and SS 7.5; beta hemolytic streptococcus PS 0.5 and SS 7.5.

Case 270. This case shows a persistence of E. coli and a positive blood culture for P. mirabilis occurring 1 week after intensive streptomycin therapy. The organism isolated from blood culture was of low streptomycin sensitivity. The effect of streptomycin therapy appears to be fleeting as the blood culture was rechecked and verified. On July 16 urine culture showed E. coli PR 400 and SS 1; paracolon PS 400 and SS 1; P. vulgaris PS 400 and SS 0.5. On August 7 the right kidney urine showed E. coli, gamma streptococcus, and A. aerogenes; while the left kidney urine showed E. coli and gamma streptococcus. The blood streptomycin level August 1 to 10 was 8 U/cc. On August 15 the blood culture was negative. On August 17 two blood cultures were positive for P. mirabilis PS 50 and SS 1; found in the urine this same day were P. mirabilis, sensitivity to penicillin and streptomycin as above; E. coli PR 400 and SR 200; enterococcus PS 50 and SR 200. On September 19 P. mirabilis had disappeared and 5 other organisms were found. On October 16 urine culture again showed 4 different organisms. On both of these dates the resistances were distributed so as to nullify treatment with antibiotics.

TABLE 3. *Case 184. Showing that organisms commonly found in urine cultures are not sensitive to tyrothricin in usable concentrations*

DATE	ORGANISM	PENICILLIN	STREPTOMYCIN	TYROTHRICIN
July 13	Paracolon	Sensitive 400 U	Resistant 200 U	Resistant 0.2 mg
	P. rhettgheri	Sensitive 400 U	Sensitive 0.5 U	Resistant 0.2 mg
	gamma streptococcus	Resistant 400 U	Resistant 200 U	Sensitive 0.5 mg
Aug. 5	Paracolon	Resistant 400 U	Sensitive 0.5 U	Resistant 0.5 mg
	Achromobacter	Resistant 400 U	Sensitive 0.5 U	Resistant 0.5 mg
Aug. 17	Paracolon	Resistant 400 U	Sensitive 7.5 U	Resistant 0.5 mg
	P. mirabilis	Sensitive 50 U	Sensitive 1 U	
	E. coli	Sensitive 300 U	Resistant 200 U	Resistant 0.5 mg
Aug. 19	Paracolon	Sensitive 50 U	Sensitive 5 U	Resistant 0.5 mg
	Achromobacter	Resistant 400 U	Sensitive 50 U	Resistant 0.5 mg
	A. aerogenes	Resistant 400 U	Sensitive 200 U	Resistant 0.5 mg
	P. vulgaris	Resistant 400 U	Sensitive 200 U	Resistant 0.5 mg
	P. ammoniae	Resistant 400 U	Sensitive 200 U	Resistant 0.5 mg
Sept. 30	P. vulgaris	Sensitive 5 U	Sensitive 1 U	
	E. coli	Resistant 400 U	Sensitive 1 U	
	Pyocyaneus	Sensitive 100 U	Sensitive 7.5 U	
	Strept. fecalis	Sensitive 50 U	Sensitive 15 U	
Oct. 11	Serum streptomycin level—40 Units/cc.			
Oct. 12	Urine streptomycin level—75 Units/cc.			
Oct. 13	Achromobacter	Sensitive 300 U	Resistant 200 U	
	A. aerogenes	Resistant 400 U	Resistant 200 U	
	Strept. fecalis	Sensitive 5 U	Resistant 200 U	
	P. vulgaris	Sensitive 300 U	Resistant 200 U	
	P. rhettgheri	Resistant 400 U	Resistant 200 U	
	P. morgani	Resistant 400 U	Resistant 200 U	

The unusual streptomycin levels on October 11 and 12 are due to renal deficiency resulting from kidney stones in one functional kidney.

Case 107. Here is an example of the persistence of paracolon bacilli and the change in bacterial flora in urine cultures over a 6 month period. On April 17, before penicillin and streptomycin sensitivities were determined routinely, paracolon bacillus, B. alcaligenes, and Staphylococcus albus were isolated. Three months later a culture of the urine showed paracolon bacilli (PS 400, SS 15) and a gamma streptococcus (PS 5, SS 200). On August 14 paracolon, A. aerogenes whose antibiotic sensitivity remained unchanged up to October 25) achromobacter and pyocyaneus were isolated, all resistant to streptomycin at 200 U/cc. One week later, August, 21 the streptomycin resistance for paracolon had changed to a sensitivity at 7.5 U/cc. Aerogenes remained unchanged but the streptomycin sensitivity of Achromobacter at 50 U/cc had changed to a resistance of 200 U/cc. Ten days later, A. aerogenes, Achromobacter, and pyocyaneus were all streptomycin resistant at 200 U/cc, a micrococcus was streptomycin sensitive at 100 U/cc. Culture on September 12 showed A. aerogenes, paracolon, and a diphtheroid; all streptomycin resistant at 200 U/cc; A streptomycin sensitive P. vulgaris at 100 U/cc also grew out. On October 1 the antibiotic sensitivity of Achromobacter had changed considerably from the date of first isolation; streptomycin sensitivity was down from a resistance at 200 U/cc to a sensitivity at 1 U. It was resistant to penicillin at 400 U on August 21, sensitive to 100 U on August 31, and to 50 U on October 1. The streptomycin sensitivity of P. vulgaris had changed from a sensitivity at 100 U on September 12 to a sensitivity of 7.5 U on October 1. Another culture was taken the following day, October 2, and the following results were obtained: Paracolon (PS 50, SS 1); Achromobacter with a penicillin resistance up from a sensitivity at 50 U 24 hours previous to a resistance at 200 U, while the streptomycin resistance jumped from a sensitivity at 1 U to a sensitivity at 200 U in the same 24 hour period; P. vulgaris was less resistant to penicillin, its sensitivity dropping from a resistance at 400 U to a sensitivity at 200 U/cc and its streptomycin sensitivity changing from 7.5 to 1 U. E. coli and enterococci were also isolated. Culture on October 25 showed A. aerogenes, Achromobacter, and pyocyaneus, all PR 400, SR U/cc.

Case 84 shows the persistence of A. aerogenes in culture over a 5 month period as well as the fluctuations in antibiotic sensitivity. The original culture on this patient was taken June 17 and showed the following organisms: A. aerogenes (PR 400, SS 50), P. vulgaris (PR 400, SS 5) and gamma streptococcus (PS 5, SS 100). One month later, on repeat culture, P. vulgaris still PR 400 but was SS 1 instead of 50 U/cc. E. coli (PR 400, SS 100), and paracolon (PR 400, SS 100). On August 15 the penicillin sensitivity of A. aerogenes had fallen, from PR 400 on June 17, to PS 2.5; the streptomycin sensitivity increased from 50 U to 300 U over the same period. The penicillin sensitivity of E. coli decreased from a resistance to 400 U on July 14 to a sensitivity to 7.5 U. Achromobacter was also isolated with a PS 1; however this organism was never isolated again on subsequent cultures. Two days later, August 17, A. aerogenes was again encountered, this time its PS had increased from 2.5 U to a resistance of 400 U while the streptomycin sensitivity dropped from 300 to 50 U/cc over the same 48 hour period. Streptococcus fecalis was also isolated. The blood streptomycin level on August 22 was 12 U/cc. On September 5 A. aerogenes, E. coli, and gamma streptococcus were all penicillin resistant to 400 U and streptomycin resistant to 200 U/cc. On November 1 the SS of E. coli and A. aerogenes had fallen to 1 U/cc. Pyocyaneus was SS 25 U/cc; all three organisms were penicillin resistant to 400 U/cc.

Case 183 is an excellent example of the apparent ineffectiveness of streptomycin in lowering the number of organisms in paraplegic urine. On 28 August E. coli were cultured from the right kidney; E. coli and P. vulgaris from the left. Serum streptomycin level on August 31 was 10.5 U/cc and the urine level on the same date was 130 U/cc. Culture on September 9 yielded but one organism, E. coli. Two days later three strains of Proteus (mirabilis, morgani, and americanus) were isolated in addition to E. coli, A. aerogenes, and Achromobacter; making a total of 6 organisms isolated from the same urine.

SUMMARY

The bacteriologic findings on urines from 274 paraplegic patients are presented.

Gram negative organisms constituted 75.6 per cent of the different types of organisms isolated.

Organism types found in urines of paraplegic tend to increase with time lapse, despite treatment.

The necessity of repeated catheterization appears to parallel reinfection despite extreme care as to cleanliness.

Antibiotic studies present a variety of findings, due to changing flora, reinfection, and acquired resistance of the organism to antibiotics.

A series of case briefs illustrates the general complexity of bacteriologic factors in the paraplegic problem.

In paraplegics, and possibly other conditions presenting mixed infections, single antibiotic sensitivity determinations as an index for therapy are of little value.

The authors express their appreciation to Miss Mary Turner, Miss Katherine Vandenboom, and Mr. Lawrence Gates, of the bacteriology section, for their assistance in assembling the data upon which this report is based.

REFERENCES

Committee on Chemotherapeutic Agents, National Research Council (Keefer, C. S. and others): Streptomycin in treatment of infections. J. A. M. A., **137:** 4–10, 1946.

Cross, W. W.: A study of 470 cases of urinary tract infections. Urol. & Cutan. Rev., **41:** 703, 1937.

Kennedy, J. A., Cummings, P. O. and Morrow, N. W.: Atypical lactose fermenters belonging to the genus bacterium (Bergey): Cultural and biochemical reactions. J. Infect. Dis., **50:** 333, 1932.

Levine, M.: Unclassifiable gram negative rods in urinary infection. J. Bact., **45:** 53, 1943.

Miller, C. P. and Bohnhoff, M.: Development of streptomycin resistant variants of meningococcus. Science, **105:** 620, 1947.

Petroff, B. and Lucas, F. V.: Streptomycin in urinary infections. Ann. Surg., **123:** 808, 1946.

Schaub, I. G.: Paracolon bacilli and their relationship to urinary tract infections. J. Lab. & Clin. Med., **31:** 958, 1946.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

A REPORT ON SEXUAL FUNCTION IN PARAPLEGICS[1]

HERBERT S. TALBOT

From the Cord Injury and Urological Sections, McGuire Veterans Administration Hospital, Richmond, Va.

No comprehensive study seems yet to have been made of the sexual function after injury or disease of the spinal cord sufficient to produce paraplegia. There is a widespread belief that all persons so afflicted are permanently and completely impotent and sterile. Available evidence indicates that this is not the case.

Direct innervation of the germinal epithelium or the interstitial secretory tissue of the gonads has not been definitely demonstrated.[2] Testicular function, seminal or endocrine, seems not to be altered by transection of the spinal cord. Although testicular biopsies or seminal studies were not prepared for this report, other evidence of continuing function has not been lacking. No atrophy of the testicle has been observed except in a few instances clearly the result of infection. There has been no impairment of secondary sexual characteristics. In the female, menstruation usually continues unchanged and gestation has been reported.[3] While this study was in progress 2 young women with cord injuries came under observation, one a paraplegic and one a quadriplegic. Both menstruate normally, retain all their feminine characteristics, and show no sign of ovarian deficiency.

The exercise of normal sexual activity, however, depends not only upon the secretory function of the gonads, but, in the male, also upon certain neuromuscular mechanisms by which the living sperm are delivered into the genital tract of the female. As regards these mechanisms, a reasonable analogy may be drawn between the sexual and micturitional functions. Both comprehend reflex acts overlaid by controls from higher centers.[4] In the presence of a cord lesion, the fundamental reflex function may be expected to persist unless there is involvement of the center itself, or of its communicating fibers. It is quite true that such reflex activity, lacking its normal controls, may be less help than hindrance, but reconditioning and readjustment are fortunately possible in many instances. The reflex, or as it is more commonly called, the "automatic" bladder is evidence alike of the dysfunction resulting from uncontrolled reflex activity, and the capacity for retraining to a fair degree of usefulness.[5] Whether the analogy can be carried as far in the case of the sexual function remains to be seen.

---

[1] Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

[2] Kuntz, A.: The innervation of the gonads in the dog. Anat. Rec., 17: 203, 1919.
Idem.: The Autonomic Nervous System. Philadelphia: Lea & Febiger, 1945, 3rd ed.

[3] Cleland, J. G. B. Paravertebral anesthesia in obstetrics. Surg., Gynec. & Obst., 57: 51, 1933.
White, J. C. and Smithwick, R. H.: The Autonomic Nervous System. New York: Macmillan Co., 1946, 2nd ed.

[4] Learmonth, J. R. A contribution to the neurophysiology of the urinary bladder in man. Brain, 54: 147, 1931.
Denny-Brown, D. and Robertson, E. G.: On the physiology of micturition. Brain, 56: 147, 1933.
Talbot, H. S. Cystometry and the treatment of vesical dysfunction in paraplegia. J. Urol. 59: 1130, 1948.

There are, of course, two reflex mechanisms involved, namely erection and ejaculation. It is generally agreed that in man the center for erection is situated in the upper one or two sacral segments. The efferent pathway is parasympathetic, the fibers passing through the visceral rami of the sacral nerves, which were for this reason called the "nervi erigentes" by Eckhardt in 1863. The ejaculatory center, according to all available evidence, is located in the upper lumbar segments; its efferent pathway is sympathetic, through the hypogastric plexus, exciting contraction of smooth muscle in the vasa deferentia, the prostate and seminal vesicles, the trigone, and the posterior urethra. There is some evidence that the lumbar center may also, to a degree, mediate erection, particularly when the excitation is of psychic origin. Reflex contraction of certain striated muscles, the constrictor urethrae, and the bulbo- and ischiocavernosus, completes the ejaculation by expelling the semen from the urethra. There is also reflex as well as voluntary activity of some of the skeletal muscles of the trunk and extremities, which has been observed in man as well as in experimental animals.[6]

In the normal human adult, the fundamental reflex nature of the sexual act is drastically modified by the influence of higher centers. Ejaculation cannot be evoked as a voluntary act, and there is no evidence of direct cortical impulses being delivered to the smooth muscle involved in erection or ejaculation. Psychic stimuli can, however, bring about or inhibit erection, with the cortical influences probably impinging upon effector neurons at the level of the center in the cord. Theoretically, since two distinct centers are involved, ejaculation should be possible without erection, and in experimental animals can be so evoked by appropriate stimulation. Normally, however, it requires a summation of stimuli which will have already produced erection. Nocturnal emissions may at times result from stimuli arising within the genital passages, and in the absence of primary erection, but such ejaculations are of no biological value so far as reproduction is concerned.

In consideration of this brief outline of the neurophysiology, certain types of alteration may be anticipated after injury of the spinal cord. 1) There may be destruction of either or both of the centers or interruption of their communicating fibers. This, of course, must result in the abolition of the mechanisms they mediate. 2) There may be complete transection of the cord above the level of the centers, with persistence of reflex activity but no manifestation of cortical influence. 3) There may be incomplete transection of the cord, with persistence of reflex function and varying degrees of cortical control.

---

[5] Talbot, H. S. A consideration of the urological care of paraplegics. Virginia Med. Monthly, 73: 449, 1946.

[6] Henderson, V. E. and Roepke, M. H.: On the mechanism of erection. Am. J. Physiol., 106: 441, 1933.
Fulton, J. F.: Physiology of the Nervous System. New York: Oxford University Press, 1943.
Marshall, F. H.: The Physiology of Reproduction. London: Longmans, Green & Co., 1922.
Riddoch, G.: Reflex functions of the completely divided spinal cord in man. Brain, 40: 264, 1917.

This report is based on a survey of 200 paraplegic patients, all males, who were carefully questioned and observed regarding their sexual status. Etiologically the cord lesions were distributed as follows:

Traumatic	190
Tumors	4
Pott's disease	1
Syphilis	1
Diabetes (arteriosclerosis)	1
Myelitis of undetermined origin	3
	200

In no case was the lesion of less than 4 months' duration; there were 20 cases of 4 to 6 months' duration, and the remainder, excepting 2, were from 6 to 45 months. The other two had been paraplegics for 22 and 19 years respectively. Of the 200 patients, 145 are still in the hospital; 5 have died, and 50 have been discharged to their homes.

Three distinct groups were recognized early in the study. The first consisted of men who had never had erection since the onset of the cord lesion; these numbered 73, or 36½ per cent of the total number. Next were those who experienced reflex erection only, in response to local stimuli; there were 85 such patients, or 42½ per cent. Finally, there were 42 patients (21 per cent) in whom erection could be evoked by either local or psychic stimulation. This grouping is indicated in table 1.

The time factor was found not to be of great significance. The restoration of sexual function is apparently coincidental with emergence from spinal shock. This, as is well known, represents a period of great variability. Three patients reported having had erections within 24 hours of injury. Generally, if function were to return at all, it had done so by the end of 6 months. This agrees reasonably well with observations of some members of the same group with respect to recovery of bladder tone. Exceptions were noted, of course. One patient had his first erection 18 months after injury, and reported returning sensation 17 months after that. Of the 20 cases with lesions of 4 to 6 months' duration, 9 were impotent, 45 per cent as against 36½ per cent for the entire 200.

The degree of completeness of the transection of the cord is obviously important, for with incomplete lesions tracts may be spared which contribute significantly to function. On the other hand, when only minimal vestiges of motor or sensory function remain, the distinction may be of no more than academic interest. Table 2 shows the distribution of complete and incomplete transections in the three groups, as determined by gross neurological findings. Among those with incomplete lesions are a few patients who can walk unassisted, and as many more who can manage with canes. The rest depend upon wheelchairs for locomotion, although an increasing number can get along on crutches for short distances. All show neurogenic dysfunction of bladder and bowel.

Erection in response to a local stimulus depends only upon an intact spinal reflex arc; there is no need to postulate the survival of tracts leading to higher centers. More than half the men responding to local stimulation only are listed as having complete lesions, and this is the case with two-thirds of those with no erections. When, however, a psychic stimulus is effective, it follows that at least some thread of a cortico-spinal tract must remain. Of the 42 patients responding to such stimulation, only 8, or less than 20 per cent, are noted as having complete transections. In these, of course, the original interpretation of the gross neurological findings was wrong. More precise methods might have yielded other evidence that the transections were incomplete. The important point is that a patient with what is to all intents a complete transection, may yet exhibit survival of this function.

TABLE 1

Group I	No erection	73	36.5%
Group II	Erection on local stimulation	85	42.5%
Group III	Erection on local or psychic stimulation	42	21%
Total		200	

TABLE 2

	TOTAL	TRANSECTION		LEVEL		
		Complete	Incomplete	Not Localized	D-11 & Above	D-12 & Below
None	73	50	23	11	26	36
Local	85	47	38	4	59 }75%	22 }53%
Psychic	42	8	34	3	20	19
	200	105	95	18	105	77

The level of the cord lesion, be it complete or incomplete, should theoretically be of no moment so long as the actual reflex centers are spared. In fact, however, this concept must be modified. The lesions are seldom sharply confined between the imaginary planes by which the segments are divided from each other. Moreover, vertical extensions, probably degenerative in character, occur with some frequency, and may confuse the neurological findings.[7] Allowing for this, the patients were divided according to whether their lesions were situated above or below a plane between the 11th and 12th dorsal segments. Those in whom a sufficiently precise localization was impossible were excluded. The results of this classification are shown also in table 2. Of 105 patients with levels at D11 or higher, 75 per cent retained the erectile reflex. Of 77 with lesions at lower levels, that is, more likely to involve the lumbar and sacral centers, only 53 per cent still showed erections.

In any discussion or evaluation of the sexual function in these men, a suitable distinction must be drawn between potency and fertility. The former, of course, is a prerequisite to the latter, but may exist without it, when testicular function is present but there is obstruction of the seminal passages. A number of these patients have had one or more attacks of epididymitis consequent upon urethral infection, and may well have become sterilized thereby. Fortunately, with a few exceptions, they are less interested in paternity than potency. Their sexual capacities are noted in table 3, where the two groups are designated "local" and "psychic" according to the type of stimulus to which there is an erectile response. All of the "psychics", of course, respond also to local stimulation.

---

[7] Guttmann, L.: Personal communication.

Among the "local" group, only 22 of the 85 experience any sensation with erection. Incidentally, these men are no more able to inhibit than to produce an erection through cortical influence. Casual stimuli, as in washing, instrumentation, or even the pressure of bed clothes, may produce priapism. Only 6 of this group were able to evoke an ejaculation by manipulation, but the figure is of no consequence because not many had made the attempt. Eleven had had nocturnal emissions, usually with no associated erotic dream, although all members of the group had normal libidinous interests on the psychic level, allowing for their general infirmities. Nineteen had attempted intercourse with successful intromission. In 4 there was ejaculation with a sense of gratification. Six others reported gratification although ejaculation did not occur and there was no sensory orgasm.

TABLE 3

	LOCAL	PSYCHIC
Total… .	85	42
Sensation	22	37
Ejaculation	2	11
Nocturnal emission	7	6
Both.	4	6
Intercourse attempted ..	19	27 (23%)
Ejaculation .	4	16 (10%)
Gratification	6	6

Apparent satisfaction in performing the sexual act, even in the absence of voluptuous sensation, was an observation of some interest. It is probable that in many cases of impotentia the patient is less distressed by the loss of pleasurable sensation than by the accompanying sense of inadequacy. Among these patients, certainly, the ability to have intercourse appears to be a source of considerable satisfaction, intellectual, if nothing else.

In the "psychic" group, the approximation to normal function is naturally more evident, since some cortico-spinal pathway remains. Thus, of the 62, all but 5 reported sensation during erections; 17 had produced ejaculations and 12 had had nocturnal emissions, usually with erotic affect. Intercourse with intromission was accomplished by 27, in 16 with complete success, in 6 more with gratification but no ejaculation.

At first glance, the total number who have had intercourse is not impressive, 46 out of 200; but this only represents those who had successful intromission.

Consideration, moreover, must be given to the fact that three-quarters of these men are still in the hospital, that many are unmarried (which deters a good many if not all) and that some have been very ill for a good part of the time. Under the circumstances, a total of 25 per cent is not too discouraging.

Once there has been a recovery of sexual function, the pattern appears to remain constant, depending as it apparently does upon irreversible neurologic changes. Two exceptions to this may be noted. The first deals with 10 patients who had anterior rhizotomies for the relief of skeletal muscle spasms. All 10, as it so happened, had previously exhibited at least reflex sexual function. In 6 it was completely abolished by the operation, and these are listed among those without erection; in 4 it was not greatly altered. As it is generally performed, the procedure is to divide the anterior roots from D12 to S1, which interrupts the reflex arcs involved in the sex function, except that if the root of S2 be spared, a mechanism for erection may remain.

The second exception involves a very small group of men, apparently impotent but with obviously incomplete lesions, in whom it has been considered that a psychic block might be responsible. One of these showed improvement after the situation had been explained.

With no intent to exaggerate its importance, the value of a reasonable degree of sexual readjustment in connection with the rehabilitation of these men is beyond question. They seem hitherto to have been more or less written off in this respect. This preliminary, and admittedly incomplete, study suggests that for many of them the door to reasonable gratification or even paternity need not be arbitrarily closed. General misconceptions about this should be corrected, and there is an obvious need for further investigation.

SUMMARY

The neurophysiology of the sexual function in the male is briefly reviewed.

In a study of 200 male paraplegics, it was found that 36½ per cent were unable to have erections; 42½ per cent have reflex erections evoked by local stimulation; 21 per cent have erections resulting from psychic stimulation.

Of the 200, 46 have had intercourse with intromission; 20 of these had ejaculations and 12 more reported gratification without ejaculation.

Since two-thirds of these patients are capable of at least a reflex erectile response, they should not be dismissed as permanently impotent.

The relation of this response to the level and completeness of the spinal cord lesion is discussed.

Cushing V. A. Hospital, Framingham, Mass.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

RUPTURE OF THE URINARY BLADDER AND PROSTATIC URETHRA[1]

HUGH T. BEACHAM

From the Departments of Urology, Louisiana State University School of Medicine and the Charity Hospital of Louisiana at New Orleans

At the Charity Hospital of Louisiana at New Orleans from January 1, 1934 to 1948 there have been 69 cases of rupture of the bladder or prostatic urethra, excluding those associated with fractures of the pelvis, intestinal perforations and surgical trauma. These exclusions were made because of the difficulty in evaluating the role of rupture in such cases. The incidence as to admissions to the urologic services was 1:395 among the male and 1:2,051 among the female patients.

The majority of cases occurred in the sixth, seventh and eighth decades. This prevalence is due to the injuries during prostatic resection in older patients and the exclusion of some cases due to external trauma among younger patients.

ETIOLOGY

Transurethral resection has resulted in 13 intraperitoneal and 33 extraperitoneal ruptures. In reviewing these charts, it was observed that rupture is more common in the resection of a large gland, and is unusual in the resection of prostatic carcinoma and contractures of the vesical neck. This may be explained by the fact that the resectionist is apt to be intent upon removing a certain amount of tissue in cases of the former while in the latter he is primarily concerned in the creation of an adequate channel. It was also notable that no ruptures were found in enucleations of the prostate gland. Twenty-eight of these accidents occurred to members of the visiting staff, while in 18 instances the resections were done by residents.

There has been an increase in the number of resections during recent years. Although the number of perforations has also increased, actually the highest incidence was during the time when resection was in its infancy.

On five occasions the tears occurred in weakened walls with the introduction of rubber catheters or with distention during cystoscopy or transurethral resection. Carcinoma and infection caused the weakness in some while in others obstructive lesions had led to very thin structures. Sounds and stylets forcibly tore through fixed portions of tissue of 4 patients.

There are only 5 gunshot wounds included. All of these were extraperitoneal, as would be expected when all with intestinal perforations were eliminated. Those occurring with blows, falls or crushing injuries numbered only 5. The smallness of this category is due to the exclusion of ruptures with associated pelvic fractures, which makes up the largest group due to external trauma. In the possible applications of the concept of lipoacid-lipobase disproportion in pathological lesions in controlled series of operative cases. The results indicate not only that this approach appears to be more efficient than other known methods of pain control, but that profound physiological changes are brought about within the area of operative trauma as reflected by the reduction in the severity of hemorrhage and improved healing.

---

[1] Read at annual meeting, Southeastern Section, American Urological Association, Hollywood, Fla., January 8, 1948.

This concept and these studies merely open the way to further investigations along this line. Much more detailed information concerning the nature of the local physico-chemical changes within pathological foci and the means of controlling such changes are necessary.

SUMMARY

A new concept of the local physico-chemical changes occurring within pathological foci as introduced by Revici, has been briefly described. According to this view, pain is the result of local *p*H changes brought about by the accumulation of acid or alkaline substances within disturbed tissues. Changes in the lipid balance are associated with and may account for these alterations.

The possibility of correcting or neutralizing such lipid changes has been explored clinically in several series of urological cases. The favorable effects upon pain as well as upon bleeding, wound healing and other important postoperative problems and complications indicate the need for further study along these lines.

54 Greene Ave., Brooklyn, N. Y.

MEETING, NEW YORK SECTION,

November 16, 1949
Yale Club, New York City
8:30 P.M.

IXED TUMORS OF THE KIDNEY IN CHILDHOOD

Dr. Robert E. Gross,
Ladd Professor of Children's Surgery, Howard Medical School,
and Surgeon-in-Chief, the Children's Hospital, Boston

Discussion: Drs. Meredith F. Campbell
and Charles T. Hazzard

Gross hematuria was common in both types of rupture, which is easily explained by considering the cause of these ruptures. However, in a few instances, particularly with external trauma, the absence of gross hematuria may have led to complacency on the part of the inexperienced observer although the microscopic presence of red blood cells in the urine should have been sufficient to prompt the proper investigation.

The low percentage of those presenting retention, even with marked intraperitoneal leakage, is explained by the fact that most of these patients were in shock. The 100 per cent finding is tenderness in the abdomen (unless it is masked by anesthesia). As disclosed by table 2, the late symptoms allow for a clearer differentiation of intraperitoneal from extraperitoneal rupture. When neglected intraperitoneal rupture leads to peritonitis with the gastro-intestinal disfunction, rigidity becomes even more pronounced and distention is the rule. The localization of pain and tenderness and the milder degree or absence of shock in the extraperitoneal type are the principal points of differentiation. Presence of shoulder pain or upper abdominal pain especially while in the Trendelenburg position indicates diaphragmatic irritation of intraperitoneal extravasation.

TABLE 2.—*Late symptoms and signs*

	INTRAPERITONEAL	EXTRAPERITONEAL
	%	%
Pain		
Severe	100	93
Localized	7	95
Generalized	93	5
G. I. symptoms	100	37
Retention	21	20
Shock	36	5
Mass	7	85
Rigidity	93	25
Tenderness	100	95
Distention	93	20

Many of these patients were under anesthesia. Fortunately practically all of them were anesthetized with a low intrathecal (saddle-type) block, which allows the patient to feel the discomfort of some extraperitoneal extravasations and certainly of the majority of intraperitoneal ruptures. It is conspicuous that at times the complaints of the patient during the operation were blamed on the ineffectiveness of the anesthesia, when actually the patient experienced rather diagnostic pain.

DIAGNOSTIC PROCEDURE

In the majority of these cases studied, it is apparent that no special diagnostic methods were necessary, inasmuch as the clinical pictures were rather typical

There were only 7 that were visualized. Perhaps this low figure is due to the failure of the operators to record their observations. The failure of the irrigating fluid to return as it should may be the first abnormality detected.

In 11 cases, cystography was utilized. In 5 it did not demonstrate the rupture; however, in each of these the technique was faulty. The most common errors were failure to take proper views to show the contour of all of the bladder or failure to properly distend the organ. Unless the technique is correct, results may lead to false security. Relatively few of these cases (6) had diagnostic catheterization alone. In several instances a quantity of fluid was injected into the bladder and the amount returned determined. Here again there were errors in interpretation because inadequate amounts of fluid were used. Should one choose this technique in determining the integrity of the bladder erroneous conclusions may be avoided by the use of amounts up to 300 or 500 cc. after smaller quantities have returned completely.

Cystoscopy was used for diagnosis in only one case; however, its proper employment constitutes a valuable aid.

OPERATIVE THERAPY

Once the diagnosis has been definitely established, or sufficient evidence is at hand to warrant suprapubic investigation, what procedure should one use? The most important consideration is to have constant drainage so as to reduce intravesical pressure and to prevent further extravasation. The extraperitoneal areas of extravasation must be drained.

At times the associated hemorrhage necessitates packing or suturing, but for the most part keeping the bladder in an empty state tends to stop hemorrhage.

Laparotomy was performed in 18 of the cases under consideration. At times this procedure was done to facilitate suturing. Rarely is it necessary, because in most instances sutures may be placed intravesically. Laparotomy is justified to empty large quantities of fluid from the peritoneal cavity, and is certainly indicated in cases where there is a question of perforation of other viscera.

An enucleation was done following 1 resection because of uncontrolled hemorrhage in the presence of extraperitoneal extravasation. This patient recovered. For 1 case perineal drainage was established. In the absence of extravasation below the urogenital diaphragm this procedure is not justified, and indeed opens a new route of extravasation and infection.

In only one of the cases operated upon was drainage of an abscessed area done without suprapubic cystostomy. Acute appendicitis occurred with extraperitoneal extravasation in one and responded after appendectomy. In another an ileostomy was performed for intestinal distension and the patient survived.

There was only 1 death in which the anesthetic was definitely thought to be at fault. The type was spinal. In recent years more general anesthesia has been used for patients in shock.

Blood administration plays an important part in the reduction of the mortality rate. During the last few years more patients have received adequate amounts of blood, but there still remain a few, even with the presence of a large blood bank, who have failed to receive sufficient quantities. The quantity of blood to be administered depends directly upon the quantity lost. Similarly the rate of administration depends upon the rate of loss.

A.—Duration before corrective surgery

(Resection cases)

SURVIVALS	TIME	FATALITIES	
		Contributory cause	Principal cause
$\boxed{X}$ $\boxed{1}$ $\boxed{1}$	1 hrs	$\boxed{X}$ $\boxed{X}$ $\boxed{X}$ $\boxed{X}$	
$\boxed{X}$	2 "	$\boxed{X}$	
$\boxed{X}$ $\boxed{X}$	3 "	$\boxed{X}$ $\boxed{X}$ $\boxed{X}$ $\boxed{1}$ $\boxed{1}$	
	4 "	$\boxed{X}$	
	5 "	$\boxed{X}$	
	6 "	$\boxed{X}$ $\boxed{1}$ $\boxed{1}$	$\boxed{X}$
$\boxed{X}$	7 "		$\boxed{X}$
	11 "	$\boxed{X}$	
	13 "	$\boxed{1}$	
	15 "	$\boxed{X}$	
$\boxed{X}$	17 "		
	24 "	$\boxed{X}$	
	72 "		$\boxed{X}$ $\boxed{1}$
$\boxed{X}$	7 days	$\boxed{X}$	$\boxed{X}$

FIG. 1. *A*, $\boxed{X}$ Represents 1extra peritoneal rupture. $\boxed{1}$ Represents 1 intraperitoneal rupture.

B.—Duration before corrective surgery

CAUSE	SURVIVALS	TIME	FATALITIES	
			Contributory	principal
Sound or Stylet	$\boxed{X}$	1 hrs.		
Cystoscopy		2 "		
or Lithopaxy	$\boxed{1}$	3 "		$\boxed{1}$
		24 "	$\boxed{X}$	
		48 "		$\boxed{X}$
		6 days		$\boxed{X}$
Catheter		3 "		$\boxed{1}$
		4 "		$\boxed{1}$
Laceration		3 hrs.	$\boxed{X}$	
Puncture	$\boxed{X}$	20 "		
Gunshot	$\boxed{X}$ $\boxed{X}$	3 "		
	$\boxed{X}$	5 "		
	$\boxed{X}$	7 "		
	$\boxed{X}$	13 "		
Falls or Blows	$\boxed{1}$	7 "		
	$\boxed{1}$	8 "		
	$\boxed{1}$	15 "		
	$\boxed{1}$	2 days		
		6 "		$\boxed{1}$
Spontaneous	$\boxed{X}$	2 "		

FIG. 1. *B*, $\boxed{X}$ Represents 1 extraperitoneal rupture. $\boxed{1}$ Represents 1 intraperitoneal rupture.

have survived 6 to 9 years without evidence of cancer, and without hormonal control.

In the 78 cases in which the growth seemed to be completely confined to the prostate, 24 patients were known to have had recurrence. Of the remainder, 40 lived or are living 5 years or longer without evidence of cancer, or a survival of 51.3 per cent. Their ages varied from 51 to 82 years, the average being 64.2 years.

The microscopic sections in these 78 cases were then examined to see how accurately one could define the limits of prostatic cancer by rectal examination. In 32 instances carcinoma had extended beyond the prostate, and in 31 of these the cells were present in the perivesicular tissues. In not a single case in the entire series were carcinoma cells found within the lumen of the seminal vesicles or vas deferens. Perineural lymphatics, however, were frequently involved. Of these 32 cases of microscopically proved extraprostatic extension, there were 16 deaths from cancer. Twelve patients lived or are living 5 years or longer without recurrence, and 4 of these have survived between 9 and 16 years. It would seem therefore that the radical operation should not be undertaken at all unless one removes intact and with a wide margin the layer of fascia covering the seminal vesicles behind and the layer covering them in front, so that the vesicles are never exposed.

TABLE 1. *Total radical operations for cancer of prostate prior to May 1, 1943: 132 cases*

LOCAL CONDITION AS DETERMINED ON RECTAL EXAMINATION	CASES	DIED WITH CANCER	DIED WITHOUT CANCER	LIVING WITH CANCER	LIVING WITHOUT CANCER
Extraprostatic extension	54	40	8 (4 lived 6 to 9 yrs.)	3*	3 (6 to 9 yrs. without castration or estrogen)
Intraprostatic (confined to prostate)	78	23 (3 over 5 yrs.)	30 (16 lived 5 to 27 yrs.)	1 (5 years, 9 mos., without castration or estrogen)	24 (6 are 10 years or more, 3 are 9–10 years; without castration or estrogen

* One, 5½ years with castration; one, 7 years, without castration or estrogen; one, 11 years, wih metastases at 9 months.

In only 41 of these 78 cases did the microscopic sections show that the carcinoma was apparently limited to the prostate. Eight of these patients subsequently had recurrence or metastases, whereas 25, or 60 per cent, have lived 5 to 27 years without cancer.

In this group of 78 cases, in which the carcinoma was not grossly extraprostatic, there were 31 cases in which a circumscribed nodule of almost stony consistency had been described lying within one lateral lobe. In only 5 of these did the microscopic sections confirm the existence of a strictly localized carcinoma. In the remaining 26, the carcinoma had extended more or less widely throughout the gland, and in 11, cells were present in the perivesicular tissues. This finding clearly indicates that if curative surgery is ever to be undertaken for prostatic cancer, the operation at all times should be made as radical as possible.

Of the 5 cases with microscopically localized cancer there has been 1 recurrence. One patient died postoperatively, and the remaining 3 have survived 9, 10, and 27 years without cancer.

Of this total group of 78 cases without preoperative evidence of extraprostatic extension, 43 were operated upon prior to May 1, 1938. Of these, 12 patients lived or are living 10 to 27 years without demonstrable cancer, a 10-year survival of 28 per cent. In 2 of these cases carcinoma cells were found microscopically in the perivesicular tissues in the removed specimen.

It is true that 2 other patients lived 11 years and 14 years, 9 months with recurrence, but this was clinically observable 9 years and 4½ years respectively after operation, and doubtless could have been detected earlier had they been examined. No patient who lived 10 years without demonstrable recurrence or metastases subsequently showed evidence of cancer. This survival rate strongly suggests that the existence of distant metastases should not be inferred merely from the finding of tumor cells in the perineural lymphatics within the substance of the prostate gland.

The operative mortality has steadily declined through the years. In the total group of 190 cases there were 12 deaths, a mortality of 6.3 per cent. These were the result of shock in 2 cases; septicemia, 2 cases; pyelonephritis, 3 cases; agranulocytosis, 1 case; hemorrhage from peptic ulcers, 1 case; pneumonia, 1 case; coronary occlusion, 1 case; and pulmonary embolus, 1 case. In the last 10 years there were 6 deaths in 127 cases. In the last 100 cases there were 3 deaths, and in the last 50, none.

Urinary incontinence has been less troublesome in the last 10 years with the utilization of Vest's method of vesico-urethral anastomosis[3] but there is still room for improvement. Vest's closure was used in 114 cases, and 36 per cent of these patients had perfect control on leaving the hospital. One hundred of these patients have been followed, and 75 eventually had perfect urinary control. Thirteen continued to have slight stress incontinence, with the loss of a few drops of urine on coughing, sneezing, or straining, insufficient to require any precautionary device. Twelve had poor control and required a urinal or clamp.

There were 7 postoperative strictures following this method of anastomosis, but all of these responded satisfactorily to simple instrumentation. In 1 case some obstruction had resulted from slight deformity at the site of anastomosis, which was corrected by a small transurethral resection.

In the total series of 190 cases there were 7 instances of rectovesical fistula, 2 of which healed spontaneously. Of the 5 persistent fistulas, only 1 occurred in the 127 cases done during the last 10 years, and followed the removal of a large carcinoma with extraprostatic extension.

[3] Vest, S. A.: Radical perineal prostatectomy, modification of closure. Surg., Gynec. & Obst., 70: 935–937 (May) 1940.

but animals are not humans, and our experience with prostatic cancer in animals is too limited to be of much value. As urologists we are all fundamentally interested in *human* prostatic cancer.

Up to the birth of the twentieth century little effort was made to differentiate benign and malignant growths of the prostate. During the years 1900–1935, the microscope and the x-ray were the only long-handled retractors of science used in this problem, but in the past decade the biological factor has been introduced which opens new possibilities for consideration of the cancer cell in its biological, physiological, chemical and morphological aspects. Strohm in 1935 discovered that the female sex hormones affected the growth of prostatic cancer cells and that the patient's pain at the site of bony metastases was relieved by the injection of placental blood. Counseller and Munger independently found that irradiation of the testes in sterilizing doses gave relief of pain in metastases from prostatic cancer. A biological relationship was thus definitely established between the gonads and prostatic cancer. This is implemented by the observation that eunuchs have never developed cancer of the prostate. The chemical side of the problem has been exposed by Kutscher, Wolbergs, the Gutmans and Sproul, who in these same years found the acid phosphatase content to be increased in cancer of the prostatic gland and in metastatic lesions from cancer of the prostate and furthermore noted the increase of the enzyme in the blood stream of patients suffering from this disease. Gomori is credited with the use of the lead stain which demonstrates the enzyme in the epithelial cells of the prostate. Huggins' experimental work has added scientific knowledge of the physiology of the prostatic epithelium of the dog. Microscopically and chemically the normal prostate in the human and the normal prostate in the dog are similar, but the benign enlargements are different: the dog's benign enlargement is an adenoma, while the human's is an hyperplasia. The human develops prostatic cancer frequently and the dog rarely if ever,—at least the author has never seen prostatic cancer in a dog. One is not justified in assuming that the prostatic epithelium of man and dog are similar, because prostatic tumors in man and the dog are biologically and morphologically different.

We believed that if we could grow human prostatic cancer we might avail ourselves of an unusual opportunity to study this cancer anew and perhaps break the stalemate in which we find outselves at the present time. The growth of human tissues outside of the body is not new, nor is the induction of morphological malignant changes in epithelium by the use of chemical agents new. In 1910, Carrell and Burrows, using a modified Harrison technique, grew human cancer cells in vitro. Seven years later Burrows, Burns and Suzuki cultured cancer tissue from the human bladder and prostate and noted the biological changes in the cells outside the body. Burrows and Kennaway attempted unsuccessfully to produce cancer of the prostate in mice by the prolonged use of estrogen, and Moore and Melchionni used chemical carcinogens of benzpyrene likewise without success. Dunning, Curtiss and Segaloff have been successful in inducing squamous metaplasia of the prostate in two inbred strains of rats by the use of methylcholanthrene; but, while the tumors metastasized to the lungs and skeletal system, they were not like the adenocarcinomas which we encounter so commonly in humans. Furthermore, these carcinogens used to produce neoplasms in animals are not as far as we know found in man, although they are being searched for in the various organs. Theoretically, androgen is a factor in cancerous growths of the prostate, and the female hormone, estrogen, contains an anticarcinogenic radical which at times and under certain conditions inhibits the growth of prostatic cancers. Cancer cells grow independently of the other cells of the organ in which they exist and demonstrate their autonomy by spreading to all parts of the host. A true neoplasm, according to Greene, is autonomous in character and should be made to grow outside of the human body provided it obtains nourishment.

With these factors in mind we have succeeded in transplanting human prostatic cancer into the eyes of guinea pigs through 16 successive generations without the selection of animals susceptible to cancer. Some of the transplanted tumors fill the anterior chamber of the eye of the guinea pig in 20 to 25 days; others lie dormant for several months and then begin to grow. It is our experience that the more cellular the tumor the greater is the likelihood of its growth. If there is much fibrous tissue associated with the cancer tissue, or if there is any infection, the transplanted tumor is dissolved and melts away. Success in obtaining these growths is attended by much care and patience. At the beginning of our experiment we transplanted prostatic cancer tissue into animals regardless of their sex but found that all the successful "takes" occurred only in the male animal up to the eighth generation with the exception of a single female stimulated with large doses of androgen. After the eighth generation, the prostatic cancer grew equally well in the male and in the female and now continues to grow regardless of the sex of the animal in which it is transplanted. It would not grow in castrated male animals, but we have been successful in growing it in pregnant females. See table 1.

Physiologically, the heterologous transplants resembled the cancerous growths which we see in our patients. Clinically, some grow fast and others relatively slow. Heterologously some of the transplants grew as much in volume in three weeks as others did in 6 to 8 months; a few appeared to lie dormant for several months and then began to grow. We tried to stimulate some of the transplants by giving the animal 1 mg. of androgen hypodermically daily at the time of transplant; but there was no demonstrable increase in the rate of growth, nor was there any microscopic change in the testes. Biologically, it would appear that testicular androgen is necessary to initiate the growth of prostatic cancer, as prostatic cancer has never been found in men castrated early in life. Analogously, we were unsuccessful in transplanting prostatic cancer to the castrated male animal, although it grew in a certain percentage of normal male animals. One female in the sixth generation was stimulated with 5 mg. of androgen per day and successfully grew the cancer. Now why did the cancer grow equally well regardless of sex after the eighth generation? The tumor apparently becomes tolerant of estrogen and indifferent to the presence of androgen, and at this stage its growth is little influenced by either male or female hormone.

Clinically, in some patients we see a dramatic favorable response to the removal of the androgen factor either by castration or by implementing the imbalance of the male and female hormones in favor of the female hormone by the administration of estrogen; other patients respond slowly and a few almost not at all in the last stages of the disease, even with most energetic hormonal treatment.

TABLE 1. *Results of heterologous transplantation of human prostatic cancer into the eyes of guinea pigs*

GENERATION	NUMBER OF PIGS		NUMBER OF TAKES		TAKES PER CENT	
	Male	Female	Male	Female	Male	Female
First	7	5	5	2–0*	71.4	0
Second	16	4	12	1–0*	75	0
Third	22	5	8	0	21.5	0
Fourth	10	1	2	0	16.6	0
Fifth	6	0	2	0	33.3	0
Sixth	7	1†	0	1†	0	100
Seventh	2	1	2	0	100	0
Eighth	12	2	6	1	50	50
Ninth	10	6‡	1	2§	10	33.3
Tenth	8	5	3	2	37.5	40
Eleventh	4	0	1	0	25	0
Twelfth	2	8	0	2	0	25
Thirteenth	5	5	0	0	0	0
Tenth*	3	4	1	1	33.3	25
Eleventh	3	5	1	2	33.3	40
Twelfth	8	9	2	3¶	25	33.3
Thirteenth	16	11	10	11	62	100
Fourteenth	5	6	5	6	100	100
Fifteenth	2	0	2	0	100	0
Sixteenth	4	2	3	1	75	50
Totals	152	80	66	32	43.4	40

* Initially "takes" but within 10–12 days regressed.

† Received 5 mg. testosterone daily for 35 days starting with day of transfer.

‡ Castrated

§ Stimulated with testosterone, 1 mg. a day.

¶ One pregnant animal.

* The tumor was lost in the first 13th generation but was picked up again in the 9th generation. Late or dormant growths in the 16th generation may increase the final percentage of "takes."

The tumors, then, both clinically and heterologously, possess different degrees of sensitivity to the female hormone.

CHEMISTRY

Although we know little about the chemistry of a cancer cell, we believe that the prostatic cancer cell offers the greatest opportunity for study of any of the various cancers because it produces the acid phosphatase in pathological amounts. Clinically, the presence of the serum acid phosphatase in the blood stream of patients with cancer of the prostate is not only worthy of recognition but can be depended upon as diagnostic evidence of dissemination of the cancerous lesion, for no other neoplasm produces pathological amounts in the blood stream. After castration or synthetic estrogenic therapy this enzyme largely disappears from the blood stream but in some patients will return in pathological amounts if the hormonal therapy be discontinued. However, it remains low in patients who have been castrated or who take estrogen continuously and who at the same time have an actively-growing prostatic cancer or a persistence of viable growth by rectal examination. When we have active growth of prostatic cancer with metastases why should we not always find an increase in the serum acid phosphatase in the blood stream? The heterologous transplants may help to explain this fact. In the third generation of transplants none of the cancer cells take the Gomori stain. Serum acid phosphatase levels were taken in a number of animals which had extensive growths filling the anterior chamber of the eye, but their blood failed to show any increase in this factor. Woodard has reported high blood levels and high tissue assay of acid serum phosphatase and in the same individuals later, after treatment, a normal blood level and at the same time little elevation in the cancerous tissue proper, although the tumor was actively growing. These observations indicated that the tumor had changed its metabolism and now produced but little of the enzyne. In most patients treated hormonally and in the heterologous transplants the tumor lost its power to produce the enzyme and at the same time became more and more refractory to the estrogenic hormone. Because a prostatic cancer does not produce an excessive amount of the acid enzyme is no sign that the cancer is under control. On the contrary it may indicate that the tumor has become more resistant to hormonal treatment and that no matter how much female hormone is given the tumor continues an active and progressive growth. Hence clinically and experimentally we find a tumor which is not only chemically different but biologically different from the original tumor.

Speculation as to the source of the acid phosphatase, whether it is derived from the cytoplasm or the nucleus of the cell, can be satisfied by a simple procedure. If one emulsifies the malignant prostatic tissue, centrifugalizes it at high speeds and stains the constituents with Gomori preparation, one finds that the amorphous cytoplasm takes a much heavier stain than does the nuclear component. This gives evidence that the cytoplasm of the cancer cell produces the acid phosphatase, while the nucleus controls the growth. Huggins has showed that androgen stimulates prostatic cell activity and acid phosphatase production. In the castrate the only other source for androgen production is the suprarenal gland. Thus we have a never-ending supply of the androgen. Huggins has furthermore showed conclusively that it is not feasible to remove the suprarenal glands in man, as death follows in a few days. Even if it were possible to control suprarenal androgen production and preserve the other functions of the suprarenal gland little advantage could be expected if the tumor was far advanced, because the heterologous transplants in later generations demonstrate the growth to be independent of either hormone.

MORPHOLOGY

Since the prostatic cancer cell changes its physiological chemistry in its struggle for independence,—that is, it loses its ability to produce the acid enzyme,—can any change in its morphology be demonstrated? The heterologous transplants thus far show no change in the microscopic appearance of the cells. All the cells reproduce themselves and appear to be of the same cell structure throughout all the 16 generations. Clinically, we have found in two autopsies a marked transformation of the primary epithelial cell to a more anaplastic cell which more or less resembles an embryonic cell,—possibly a sarcoma cell (figs. 1, 2). One has the right to ask whether or not these cancers, if allowed to live a long time, take on an embryonic form morphologically. Greene has clearly demonstrated that human embryonic tissue from any organ will grow heterologously up to the fifth month. Both prostatic cancer and human embryonic tissue possess heterologous transplantability, while normal adult tissue can not thus be grown. Scientists who pin their faith on an embryonic factor inherent within the prostatic epithelial cell which causes a normal cell to alter its morphology would here find support of their hypothesis. Whether our heterologous prostatic

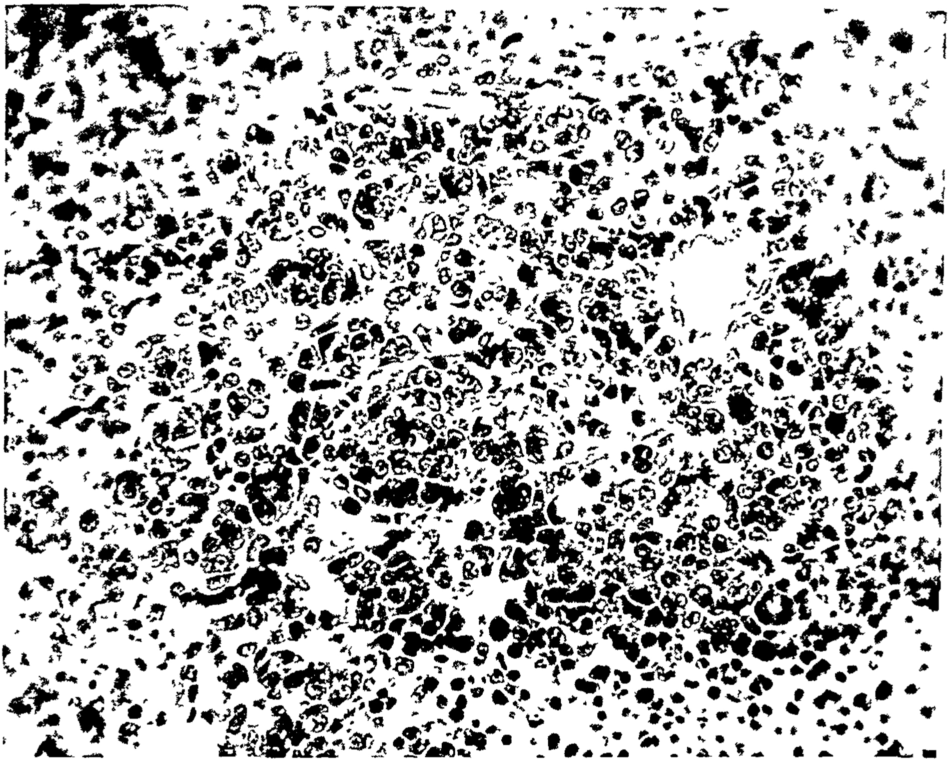


FIG. 1. J. L., aged 83, New Haven Hospital Unit No. B 30456. Castrated 5-29-42; died 2-26-45. General condition improved for 2 years. Nine months' decline before death. Autopsy.

Photomicrograph, × 300. Prostatic specimen, transurethral resection 6-17-42, two weeks after orchidectomy. Strands of prostatic epithelium mixed with dense fibrous stroma. Nests of solid masses of epithelial cells containing a scant amount of cytoplasm with abnormally large, deep-staining nuclei.

cancer growths will in future generations change to cells of embryonic character we can not predict.

HORMONAL THERAPEUSIS

When the hormonal treatment for cancer of the prostate was first instituted most observers recorded that about 80 per cent of patients responded favorably in one way or another. We have learned from the heterologous growths of prostatic cancer that in the animal the tumor becomes refractory to the ordinary amounts of estrogen. This suggested that larger doses of estrogen be employed clinically. Now with larger doses of estrogen, with or without castration, the percentage of patients who obtain relief of pain for a short period is almost 100 per cent. This observation supports the hypothesis that some patients either require a larger amount of female hormone to produce a regressive change in the cancer or that their cancers have acquired a resistance to the hormone so that larger doses of the hormone must be given to effect a favorable response. What constitutes a small and large dose of hormone is subject for discussion. We have for convenience designated any dose under 10 mg. per day a minimal dose and any over 40–50 mg. per day a large dose. However, some physicians are reported as giving 300 mg. per day. Gardner has demonstrated that small doses of estrogen stimulate the epithelial breast tissue in mice, but that large

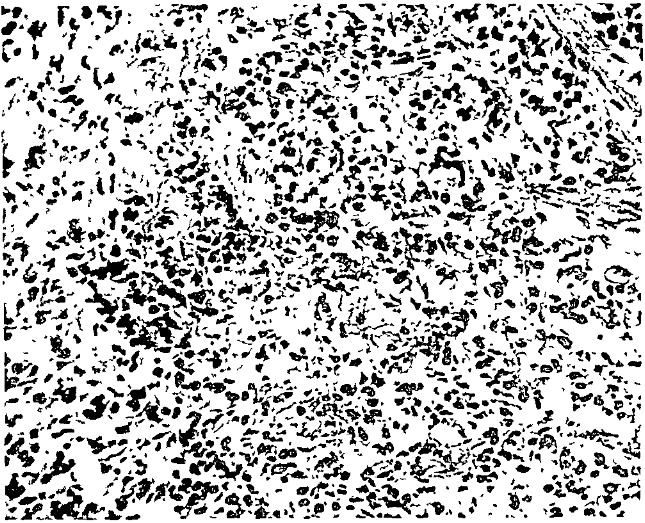


FIG 2 Photomicrograph, × 300. Specimen of prostate obtained at autopsy, 2-26-45. Very little stroma with large rounded cells containing a relatively large amount of cytoplasm and large nuclei. Note change of small epithelial cells to anaplastic embryonic type cell.

doses cause an atrophy of these tissues. The action is paradoxical, and it may be true that the female hormone acts on certain epithelial tissues as a carcinogenic agent, that different amounts of the hormone may act as an anticarcinogenic agent, and that somewhere in between large and small doses we may find the maximum desired effect without carcinogenic action. We have observed with diligence the response with respect to relief of pain as one of the main indicators as to how much hormone to administer. Patients reach levels of hormonal treatment, so that some respond well on 5 mg. per day for a while and then, as symptoms of pain recur or there is an increase in activity in the growth of the tumor, the hormone is increased until the pain disappears. We do not believe that the size of the enlarged breasts is any indicator as to the amount of hormone to be administered for the control of the tumor locally. Usually large breasts develop in castrates who receive 1 to 5 mg. of estrogen per day, but the breasts do not become so large in patients who take large doses of estrogen. None of our patients have developed cancer in their breasts following hormonal therapy. One patient who was castrated and who has received 5 mg. per day of stilbestrol for 4 years has complained of large breasts and that one breast was hard. To palpation it was hard and slightly reddened, but the hardness and redness subsided within 2 weeks after stopping the hormone and have not recurred 3 months after resuming the treatment. However, the patient insists on having his breasts removed, as he fears too much humiliation in competition on the beach during the summer months. Abramson and Warshawsky have reported 1 case of apparent carcinoma of the breast following a dosage of 1 mg. of stilbestrol per day for 14 months. No carcinomas of the breast in prostatic cancer patients have been reported after prolonged treatment with large doses of the hormone. The above reported case might be considered a primary breast tumor which had no particular relationship to the hormonal therapy.

The heterologous growth of human prostatic cancer has indicated that the transplanted cancer in the early generations is definitely influenced by hormonal factors. It would seem that androgen or one of its constituents must be present to initiate the growth of prostatic cancer but that the actual amount of androgen needed may be extremely small, because the tumor grew just as rapidly in control animals as in testosterone-stimulated males. We have learned that the physiology of the prostatic cancer cell changes in successive generations of transplants, and we have observed in some cases clinically that the morphology of the cell reverts towards an embryonic character. Biologically, the longer the prostatic neoplasm grows the more independent its cells become of hormonal environment. Clinically, we see prostatic cancer showing a wide variation of response to castration. Cancers of the prostate in some individuals are extremely sensitive and seem almost to require testicular androgen to continue growth, while others are refractory even after removal of the gonads and administration of estrogenic therapy. Clinical and experimental observations have demonstrated that the removal of the testicular androgen can not be depended upon to control prostatic cancer. The supplemental administration of as little as 1 mg. of estrogen per day is apparently sufficient to control some of the cancerous growths, while large doses do not control others. Hormonal treatment alone then does not give us the answer to the cure of cancer of the prostate. While we do not know the cause of cancer of the prostate we strongly suspect that the prostatic epithelial cells contain an embryological factor which may be the basic element in prostatic cancer growth when influenced by some constituent of the testicular androgen which "sets off" the growth or causes the apparently normal prostatic epithelial cell to change its morphology and to achieve the capacity for growth independent of its host. Hypothetically, if there are two or more factors which cause cancer of the prostate may we not be required in our treatment of prostatic cancer to counter with two or more agents to fully control the growth of such a tumor? We now know clinically and experimentally that the increase of the female hormone or the diminution of the male hormone will produce certain degrees of regression of most prostatic cancers, but the study of the heterologous growth of this tumor indicates that we need something else or some other factor to control human prostatic cancer.

SUMMARY

There is little evidence that there has been any improvement in the percentage of control of cancer of the prostate by hormonal therapy.

Human prostatic cancer can be transplanted heterologously.

Heterologous growth of human prostatic cancer in guinea pigs shows the tumor to present the same characteristics as are seen clinically.

Physiologically, it shows great variation in rate of growth.

Biologically, it would appear that testicular androgen is necessary to initiate the growth of prostatic cancer.

Clinically and heterologously prostatic cancer shows great variation in response to the female hormone.

Chemically it loses its acid enzyme production after estrogen therapy and after heterologous transplantation.

Morphologically the heterologous growths have showed no change in sixteen consecutive generations.

Clinically two tumors have showed morphological changes simulating an embryonic cell.

Removal of testicular androgen can not be depended upon to control prostatic cancer.

Prostatic cancer clinically and heterologously after varying periods of growth becomes tolerant of estrogen, which suggests that the greatest effect from its use may be expected by greater hormonal unbalance applied early in the disease.

Hormonal therapy must be more efficiently applied or it must be implemented by another agent which will completely control the growth of cancer of the human prostate.

789 Howard Ave., New Haven 4, Conn.

REFERENCES

ABRAMSON, W. AND WARSHAWSKY, H.: Cancer of the male breast secondary to estrogenic administration. J. Urol., **59:** 76, 1948.

BURROWS, M. T., BURNS, J. E. AND SUZUKI, Y.: Studies on the growth of cells. The cultivation of bladder and prostatic tumors outside the body. J. Urol., **1:** 3, 1917.

BURROWS, H. AND KENNAWAY, N. M.: On some effects produced by applying estrin to the skin of mice. Am. J. Cancer, **20:** 48, 1934.

CARREL, A. AND BURROWS, M. T.: Cultivation in vitro of malignant tumors. J. Exper. Med., **13:** 571, 1910.

Connecticut State Department of Health, Division of Cancer: Figures with respect to deaths in United States in 1946 from cancer of the prostate.

COUNSELLER, V. S.: Discussion on paper by W. E. Herrell on ophorectomy in cancer of the breast. Proc. Staff Meet., Mayo Clin., **11:** 788, 1936.

DEMING, C. L. AND HOVENANIAN, M. S.: Hormonal factor in heterologous growths of human prostatic cancer. J. Urol., **59:** 215, 1948.

DUNNING, W. F., CURTISS, M. R. AND SEGALOFF, A.: Methylcholanthrene squamous cell carcinoma of the rat prostate with skeletal metastases and failure of the rat liver to respond to the same carcinogen. Cancer Research, **6:** 256, 1946.

GARDNER, W. U.: Hormonal imbalance in carcinogenesis. Presented before New England Cancer Society, New Haven, Conn., May 23, 1947.

GOMORI, G.: Distribution of acid phosphatase in the tissues under normal and pathologic conditions. Arch. Path., **32:** 189, 1941.

GREENE, H. S. N.: Heterologous transplantation of embryonic mammalian tissues. Cancer Research, **3:** 809, 1943.

GREENE, H. S. N.: Heterologous transplantation of mammalian tumors: the transfer of human tumors to alien species. J. Exper. Med., **73:** 475, 1941.

GUTMAN, E. B., SPROUL, E. E. AND GUTMAN, A. B.: Significance of increased phosphatase activity at the site of osteoplastic metastases secondary to carcinoma of the prostate gland. Am. J. Cancer, **28:** 485, 1936.

HARRISON, R. G.: Observations on the developing living nerve fiber. Proc. Soc. Biol. & Med., **4:** 140, 1907.

HOVENANIAN, M. S., AND DEMING, C. L.: Heterologous growth of cancer of the human prostate. Surg., Gynec. & Obst., **86:** 29, 1948.

HUGGINS, C. AND CLARK, P. J.: Effect of castration and of estrogen injection on the normal and on the hyperplastic prostate glands of dogs. J. Exper. Med., **72:** 747–762, 1940.

HUGGINS, C. AND HODGES, C. V.: Studies on prostatic cancer; effect of castration, of estrogen and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate. Cancer Research, **1:** 293, 1941.

HUGGINS, C. AND SCOTT, W. W.: Bilateral adrenalectomy; clinical features and urinary excretion of 17-ketosteroids and estrogen. Ann. Surg., **122:** 1031–1041, 1945.

KUTSCHER, W. AND WOLBERGS, H.: Prostataphosphatase. Ztschr. f. physiol. Chem., **236:** 237, 1935.

MOORE, R. A. AND MELCHIONNI, R. H.: Production of tumors of the prostate of the white rat with 1-2 benzpyrene. Am. J. Cancer, **30:** 731, 1937.

MUNGER, A. D.: Experiences in the treatment of carcinoma of the prostate with irradiation of the testicles. J. Urol., **46:** 1007, 1941.

STROHM, J. G.: Carcinoma of the prostate, a study of 429 cases. Urol. & Cutan. Rev., **45:** 770, 1941.

WOODARD, H. Q.: Interpretation of phosphatase findings in carcinoma of the prostate. New York State J. Med., **47:** 379, 1947.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

INTERSTITIAL CYSTITIS: REPORT OF 223 CASES (204 WOMEN AND 19 MEN)[1]

JOHN R. HAND

To paraphrase Hunner's opening remarks to the American Gynecological Society, on May 16, 1918, it is with misgiving that I present a review on a subject with which all of you are familiar—interstitial cystitis. Nevertheless, for many years I have been impressed by the number of patients with interstitial cystitis who have had concurrent gallbladder disease, motor bowel disturbance, allergies of various kinds, and multiple pelvic operations. This study was undertaken, therefore, to determine the incidence of these and other disease processes associated with interstitial cystitis.

For some time, I have also been impressed with the inadequacy of the many names which have been given to this bladder disease. And after considerable thought, I am inclined to agree with Folsom's pithy comment that when Hunner "delivered this child into the urologic world he did not name it as well as he described it." Without doubt, some phase of the disease gives justification for each of its many names. But no one name yet proposed is wholly satisfactory because it fails to take into account the changing picture of the disease. However, until a better name is found, "interstitial cystitis" is the most suitable since it is the only name with sufficient latitude to cover a diagnosis of the early as well as the late stages of the process.

Diagnosis of interstitial cystitis is another vexing problem. Every urologist who has studied patients with this disease will agree that its diagnosis is not always apparent at the initial cystoscopic examination. Indeed, it is sometimes necessary to repeat the examination before the diagnosis can be made with certainty. Therefore it is well to bear in mind that while the presence of characteristic lesions gives unequivocal confirmation of the disease, their absence does not necessarily rule it out.

I have frequently observed that what appeared to be a normal mucosa before and during the first bladder distention showed typical interstitial cystitis on subsequent distention. Because of this, I am convinced that if we are to avoid overlooking the early lesions of interstitial cystitis the bladder should be distended, emptied, and distended a second time. It is important to remember this. However, the mucosa must be inspected thoroughly during the first distention. Otherwise, when the bladder is emptied and redistended the resultant bleeding may become so profuse that any associated lesions will be obscured.

In the differential diagnosis consideration must be given to areal cystitis, simple ulcers of pyogenic origin, tuberculosis, infiltrating carcinoma, irradiation cystitis, syphilis, bilharziasis (schistosomiasis), and amebic cystitis. Appropriate laboratory tests, biopsy, and response to specific treatment should leave no doubt as to the correct diagnosis of these conditions.

---

[1] Presidential address read at annual meeting, Western Section, American Urological Association, Victoria, B. C., April 20, 1948.

ANALYSIS OF CASES

In this series of interstitial cystitis there are 223 patients, 204 women and 19 men. All were observed by me in The Portland Clinic, from January 1930 through December 1946. During this 17 year period, 4,647 Clinic patients (5.06 per cent) had cystoscopies. Thus the 223 patients with interstitial cystitis represent 4.79 per cent of all the patients who had urologic studies in the Clinic during the period covered by this report.

Diagnostic criteria. Comparison of the recorded cystoscopic findings with the clinical histories disclosed at once that a common denominator would not be easy to establish. In some instances the cystoscopic picture did not show the degree of involvement suggested by the symptoms. In others, one or more of the classical symptoms were missing, but the findings on cystoscopy left no doubt as to the diagnosis. Yet, in spite of the difficulty in correlating examination findings with clinical evidence, definite patterns could not be ignored.

Consequently, 3 arbitrary grades were set up in accordance with the cystoscopic findings, and each of the cases was evaluated on this basis. Engel, Meads, and O'Conor also divided the cases in their series into the stage of lesion involvement.

I had no difficulty in segregating the lesions of grade 3. They were all far advanced. But the distinction between grades 1 and 2 was often difficult to make because of discrepancies in or overlapping of some of the grading criteria.

As finally determined, grade 1 represents minimal bladder involvement. On distention there were small, discrete, submucosal hemorrhages, showing variations in form. Near the trigone, for example, there were dotlike bleeding points. On the walls the bleeding areas were often single or parallel linear streaks. Occurring chiefly in the trigone and base, however, the lesions caused little or no restriction to bladder capacity. They might be likened to a posterior duodenal wall ulcer that is fixed and does not cause obstruction.

Grade 2 represents a more advanced stage of the disease. The lesions were larger, and they gave the impression of a localized edema of the bladder walls. On distention bleeding points could be seen in the thinned out mucosa overlying the edematous areas. The most frequent sites of involvement were the walls. Bladder capacity was considerably diminished. To use the same analogy, grade 2 lesions are like an ulcer on the distensible anterior wall of the duodenum. The anterior wall ulcer contracts and causes obstruction. The grade 2 lesions of interstitial cystitis, also situated on a distensible wall, contract and cause diminution in bladder capacity.

Grade 3 represents the most advanced stage of the disease. In the greatest number of cases the lesions were recorded as being "diffuse." The mucosal surface was pale and often showed linear scars of old lesions. While there was bleeding on distention, the dominant finding was a zigzag fissuring which suggested a split along the lines of the underlying vascular network and muscle bundles. Bladder capacity was greatly diminished, being 150 cc or less.

With these criteria, 138 women had grade 1 lesions; 37 had grade 2 lesions; and 29 had grade 3 lesions. Fifteen men had lesions of grade 1, and the other 4 *had grade 2 lesions. In no instance did the lesions of the men reach the same* degree of severity as those of the women.

The subsequent statistical studies were made, for the most part, on the basis of the lesion grades outlined. As an additional yardstick in evaluating the results in some of the factors analyzed, the case histories of an equal number of women and men were taken from the general Clinic admission for comparative study. These control patients had been registered consecutively and were within the age limits of the interstitial cystitis patients. They represented patients who ordinarily consult an internist, a surgeon, a gynecologist, an orthopedist, or a neurologist.

Sex. In this series, as in those of Cristol et al., Eaton, Engel, Higgins, Peterson and Hager, among others, the majority of the patients were women. The ratio was 11 to 1 (204 women and 19 men). In 708 cases of carcinoma of the bladder that I reviewed with Judd, there were 127 women and 581 men, a ratio of approximately 1 to 4.

Social status. Of the 204 women with interstitial cystitis, 176 (87 per cent) had been married one or more times, and of these 8 were widowed and 11 divorced or separated. The remaining 28 women (13 per cent) were single. Eighteen (94 per cent) of the men were married. The occupations of both men and women represented practically every field of work.

Age. Nineteen women and 2 men gave histories of childhood urinary problems. *Eight of the women and both men had enuresis. Excluding these 21* patients, the youngest woman was 13 and the oldest 73, the youngest man 21 and the oldest 60 when the symptoms of interstitial cystitis appeared.

Analyzed according to extent of involvement, the women with grade 1 and 2 lesions had symptoms at an average age of 35.5 years, and came for diagnosis approximately 7½ years later. But women with grade 3 lesions were older when symptoms began, 41 years, and came for diagnosis after a longer interval, 12½ years. The men with the advanced lesions also began to have symptoms later and came for treatment later than those with minimal lesions.

Symptoms. The symptoms in the respective lesion groups did not differ in type but rather in incidence and severity (table 1). Suprapubic pain, for example, occurred with practically the same frequency in each group, but it varied from "slight" to "intolerable." In 64 instances there was referred pain to a neighboring region, and in a few instances it was present without urinary symptoms. The pathways by which pain from the bladder and urethra is referred to surrounding structures are summarized by Wilson and Mussey.

Sixteen women and 4 men had no nocturia at the time of their initial examinations. They later developed this symptom, however, indicating a progression of the disease which was confirmed on subsequent study.

Temporary relief from previous treatment may be the explanation for the fact that not all the patients gave histories of symptoms usually associated with the disease. For example, 34 women and 4 men said they had consulted a urologist at some time before they came to the Clinic and 43 women and 5 men had previously seen a general practitioner for their bladder symptoms.

Furthermore, early symptoms of interstitial cystitis are often masked by concurrent disease processes which take the patient to the general practitioner, internist, gynecologist, obstetrician, orthopedist, or general surgeon. Support of this is the observation that 56 per cent of the women and 73 per cent of the men in this series first consulted Clinic physicians in other than the urologic department. These patients were later sent to me for completion of their clinical studies or to rule out persistent, unexplained pain. The fact that so many of these patients were referred to me by my associates may explain why I found such a large number of minimal lesions. It may also explain why I saw so many patients before pain became the dominant symptom.

TABLE 1. *Presenting symptoms*

SYMPTOMS	GRADE 1 LESIONS				GRADE 2 LESIONS				GRADE 3 LESIONS	
	138 women 15 men				37 women 4 men				29 women 0 men	
	Women	%	Men	%	Women	%	Men	%	Women	%
Day frequency	128	92.75	13	86.66	36	97.29	4	100.00	28	96.55
Night frequency	113	83.33	10	66.66	36	97.29	4	100.00	28	96.55
Gross hematuria	27	19.57	2	13.33	11	28.20	3	75.00	7	24.13
Burning	20	14.49	3	20.00	9	24.32			7	24.13
Urgency	32	23.00	3	20.00	15	40.54	2	50.00		
Incomplete emptying	18	13.00	4	26.66	7	10.00	3	75.00	4	13.00
Incontinence	10	7.00	1	6.66	2	5.00				
Suprapubic pain	53	38.40	3	20.00	15	40.54	1	25.00	12	41.03
Back pain	23	16.66	4	26.66	2	1.37	1	25.00	2	6.89
Pain RLQ	8	5.79			2	1.37				
Pain LLQ	2	1.45			1	2.7				
Pain to groin	1	.72	2	13.33	1	2.7			1	3.44
Pain to thigh	5	3.62	1	6.66					1	3.44
Pain to vagina	2	1.45							1	3.44
Pain to perineum	1	.72	1	6.66			1	25.00		
Pain to rectum	1	.72								

A number of patients associated their urinary symptoms with some initiating or aggravating cause. That is to say, menstrual periods, pregnancy, or the menopause were listed by 36 patients; food, drink, or spices of some kind by 13; nervous upsets by 12; acute upper respiratory infections by 8; gastro-intestinal upsets by 3; long automobile rides by 3; diabetes by 3; a sterilization dose of radium by 1; and a ruptured bladder in childhood by 1.

Urologic studies. The results of the initial urine and kidney function tests, as well as the roentgen and physical changes observed at the diagnostic cystoscopies, are summarized in figure 1. Most of the patients had guinea pig studies. None showed tubercle bacilli. Six women had associated glycosuria. Twenty-three per cent of the women and 21 per cent of the men had pyelonephritis (Higgins reported renal infection in 19 per cent of his 100 patients). Of the 144 urine cultures from the right and 142 from the left kidneys of the women in my series, 29 and 25, respectively, contained bacteria. Eighteen of the men had cultures of urine from both kidneys. Bacteria were found in 9 cultures from the right and 10 from the left kidney.

Blood studies. The hemoglobin rates (Sahli) of the women ranged from 55 to 115 per cent. Ten were below 80. All the men had rates above 90, the highest being 119 per cent. Two women and 1 man had positive serologic reactions and were subsequently given antiluetic treatment.

Lesion distribution. Most of the minimal lesions were found in the trigone-base area, whereas the greatest number of the advanced lesions involved either the whole of the bladder or were confined to the dome (table 2). In 17 instances (14 women and 3 men) the lesions were single. In all other instances they were multiple.

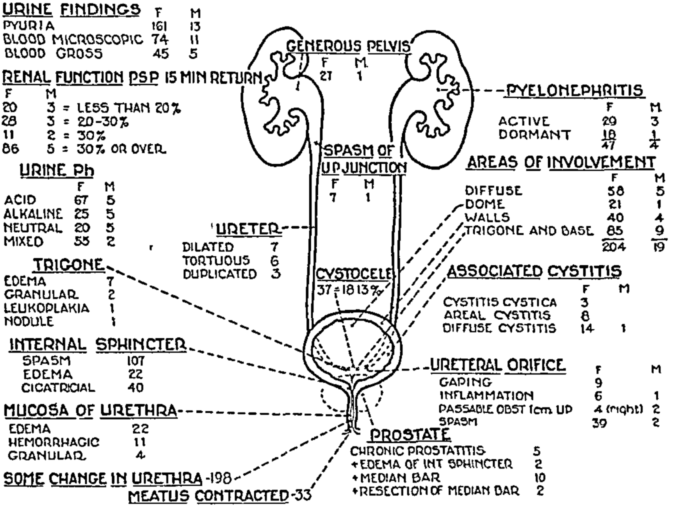


FIG. 1. Kidney, ureteral, bladder and urethral findings in 19 men and 204 women with interstitial cystitis.

Concurrent diseases and results of comparative studies. Colds, influenza, dental sepsis, jaundice, and pleurisy were more frequent among the patients with interstitial cystitis than among those in the control group. Except for these, there was practically no difference in the incidence of infection in the two groups.

The patients with interstitial cystitis had a high incidence of operations for associated disease processes (table 3). Six operations were done for carcinoma. One of the malignant lesions was in the bladder. Bumpus, Howard, Rusche and Hager, and Vose and Dixey observed carcinomatous changes in bladders involved with interstitial cystitis, 2 cases in each instance. Hagner also reported such a case and cited another mentioned by Hunner.

Leading the list of operations by a considerable margin are the pelvic proce-

Furthermore, early symptoms of interstitial cyst
current disease processes which take the patie
ternist, gynecologist, obstetrician, orthope
this is the observation that 56 per cent
in this series first consulted Clinic
ment. These patients were
studies or to rule out per
these patients were re
such a large numb
patients before pain

SYMPTOMS	Wome					
Day frequency	128	9.				
Night frequency	113	83.				
Gross hematuria	27	19.5				
Burning	20	14.49				
Urgency	32	23.00	[illegible]			
Incomplete emptying	18	13.00	4			
Incontinence	10	7.00	1	[illegible]		
Suprapubic pain	53	38.40	3	20.		
Back pain	23	16.66	4	26.6		
Pain RLQ	8	5.79				
Pain LLQ	2	1.45				
Pain to groin	1	.72	2	13.33	1	
Pain to thigh	5	3.62	1	6.66		
Pain to vagina	2	1.45				
Pain to perineum	1	.72	1	6.66		
Pain to rectum	1	.72				

A number of patients associated their urinary symptoms wi
or aggravating cause. That is to say, menstrual periods, pre
menopause were listed by 36 patients; food, drink, or spices of som
nervous upsets by 12; acute upper respiratory infections by 8; gast
upsets by 3; long automobile rides by 3; diabetes by 3; a sterilizati
radium by 1; and a ruptured bladder in childhood by 1.

Urologic studies. The results of the initial urine and kidney function
as well as the roentgen and physical changes observed at the diagnostic cy
copies, are summarized in figure 1. Most of the patients had guinea pig studi
None showed tubercle bacilli. Six women had associated glycosuria. Twenty-three per cent of the women and 21 per cent of the men had pyelonephritis (Higgins reported renal infection in 19 per cent of his 100 patients). Of the 144 urine cultures from the right and 142 from the left kidneys of the women in my series, 29 and 25, respectively, contained bacteria. Eighteen of the men had cultures

women with the bladder disease had fibroids for which operation had not been done as against 17 women in the control group (table 5) The incidence of cystoceles was also higher in the interstitial cystitis group (table 5)

TABLE 4 *Comparative incidence of pelvic operations*

PRIMARY PELVIC OPERATIONS	204 WOMEN INTERSTITIAL CYSTITIS			204 WOMEN GENERAL ADMISSION		
	History of op	After diag	Total	History of op	After diag	Total
Hysterectomy	35	6	41	11	4	15
Myomectomy	2		2			
Suspension (20 pts had 22 ops)*	20		20	11	1	12
Oophorectomy (21 pts had 24 ops)*	21		21	10		10
Salpingo oophorectomy	9	2	11	10		10
Salpingectomy	6		6	3		3
Tubes tied	1		1	1		1
Cervical operations (14 pts had 15 ops)*	14	4	18	3	2	5
Perineal repair	6		6			
Urethral caruncle removed (3 pts had 4 ops)*	3		3			
Total	117	12	129	49	7	56

* These were all patients in the interstitial cystitis group Thus 129 patients had 135 operations

TABLE 5 *Incidence of various disease processes*

CONCURRENT DISEASE	INTERSTITIAL CYSTITIS			GENERAL ADMISSION		
	Women	Men	Total	Women	Men	Total
Nonsurgical gallbladder disease*	41	5	46	20	6	26
Motor bowel disturbance	34	1	35	30	2	32
Nonsurgical thyroid disease	14		14	14	2	16
Nonsurgical fibroids	21		21	17		17
Cystocele*	37		37	15		15
Hemorrhoids	65	4	69	54	8	62
Allergies of various kinds*	32	1	33	19		19
Varicose veins	22	2	24	19	1	20
Glomus tumors†	2		2			

* Considerably higher incidence in patients with interstitial cystitis

† These two cases represent 33 per cent of the total number of glomus tumors seen in the Clinic

Since 36 women had attributed the onset of their bladder symptoms to some phase of their menstrual lives, a comparative study was made of the menstrual cycle, pregnancies, and menopause in the two groups of women There was no significant variation in menstruation nor in pregnancies In each group about one fourth of the married women had never been pregnant and approximately one-third had had abnormal pregnancies. However, there were 36 castrates among the women with interstitial cystitis (32 surgical and 4 radium) as against only 14 (surgical) in the control group. The castrates in both groups sought treatment 10 years earlier than the women who had had spontaneous menopauses.

Clinically the bladder irritability of many women with interstitial cystitis appeared to parallel the peak curves of estrogen production, that is, during ovulation and just before the period when there is retention of sodium and water and increased vascularity of the pelvic organs.

"Nervousness" was considered of sufficient importance to list with their presenting complaints by 78 women (38.23 per cent) and 4 men (21.05 per cent) with interstitial cystitis. Four women also gave histories of "nervous breakdown." A few admitted an excessive tendency to worry. Several had domestic problems. At the conclusion of the various studies of these patients, the diagnoses of 18 women and 1 man included either reactive depression, hysteria, psychoneurosis, or anxiety tension state. Thirty-eight women, but no men, in the control group had similar diagnoses. Nevertheless, while the psychogenic diagnosis was secondary for all the patients with the bladder disease, it was the primary finding for 10 women in the control group.

Allergies were more common among the patients with interstitial cystitis than among those from the general admission (table 5). Other disease processes showed no appreciable variation (table 5). Abnormalities in basal metabolic rates and blood pressure readings were noted in both groups. But the numbers were not large enough to be significant.

Treatment. The variety of therapeutic measures carried out on my patients reflects the difficulties reported by others in controlling the disease. However, treatment in each instance was approached from the standpoint of the patient's general condition as well as the bladder problem.

General management was begun with an explanation of the various factors involved in this bladder disease. Stress was placed on the difficulties of its control, emphasizing the customary remissions and recurrences. The object of the explanation was to teach the patient to "live" with the disease, for interstitial cystitis, like duodenal ulcer and ulcerative colitis, may become a lifelong problem.

Attention was next given to the correction of associated diseases, including foci, allergies, bowel irregularities, faulty posture, poor muscle tone, obesity, and undernutrition. Vitamins were prescribed for specific deficiencies. Recently, excessively nervous and tense patients have been advised to read Jacobson's book: "You Must Relax."

Women who had increased bladder discomfort during ovulation or just before menstruation were told to limit salt intake at this time and to take enseals of ammonium chloride, 7.5 grains 4 times a day.

Menopausal symptoms, which are due to estrogen withdrawal, were treated with stilbestrol, 0.1 mg. daily, as suggested by Rogers. The associated negative protein balance and mineral imbalance, accompanying long continued estrogen withdrawal, were corrected, respectively, with an adequate protein diet and calcium with viosterol.

Potassium iodide appeared to produce prolonged remission of the bladder symptoms of some patients Starting with a drop a day, the dosage was increased a drop each day until the patient was taking 15 drops daily This dosage was then continued for six weeks

Local treatment was directed toward the acuteness of the mucosal lesions, the resistance at the bladder neck, and the irritability of the detrusor muscle with the resultant diminution in bladder capacity In every instance the urethra was dilated and the bladder distended with warm boric acid solution When indicated, warm silver nitrate solution was used after local anesthesia The strength of the solution depended upon the degree of cauterization deemed advisable A 1 per cent solution was usually sufficient Before the silver nitrate was instilled, care was taken to lavage the bladder with water so that no chlorides would remain to be precipitated as silver chloride

The number and frequency of the treatments were gauged by the patient's clinical response In most cases they were given at 6 week intervals during the first year of observation Some patients, however, required more frequent treatments Often after the silver nitrate was used, 1 ounce of cajandol was instilled into the bladder and allowed to remain In some instances the cajandol was still in the bladder when the patient returned for treatment at the end of 7 or 10 days

Large areas of subepithelial involvement, that bled on distention, were carefully and completely fulgurated Some patients who had had treatment with both silver nitrate and fulguration preferred fulguration

Bladder contracture, which is a major problem in far advanced lesions, was treated by dilatation under spinal anesthesia On occasions, the desired degree of dilatation was maintained for 10 minutes

Whenever the patient complained of burning urination, 5 minim capsules of sandalwood oil were given 4 times a day Because of its surface tension properties, this drug diminishes the irritation of the urine on the bladder wall

In addition to the measures mentioned, sulfonamides were given to 46 women and 5 men Six women could not tolerate the drug The other patients, who had associated infections, noticed diminution in urinary frequency Penicillin was given to 3 women for intercurrent infection But the drug had no effect on the urinary symptoms

Recently the acute flare ups of 2 women were relieved by diathermy treatments, which were given daily for 7 and 10 times, respectively

Resection of interstitial cystitis lesions, as proposed by Folsom, Fronts, Hunt, was not done in any instance in this series because of the unfavorable conclusions reached by the advocates of the procedure after a critical study of end results One woman gave a history of having had such an operation, without relief of symptoms The reason for the ineffectiveness of this treatment is apparent when one considers the widespread distribution of most of the lesions

Roentgen therapy was also not used Kreutzmann's report indicated that the improvement with this treatment is no better than with fulguration In his series there were no permanent cures As he emphasized, the disadvantage of the treatment is that it causes cessation of menstruation

One woman consented to resection of the presacral nerve, as advocated by Learmonth. Six months later she reported the nerve section had alleviated a sharp, stabbing urethral pain that used to come without warning. When I asked if, knowing of this benefit, she would again submit to the procedure, she immediately replied she would. However, she had lesions of the grade 3 type, and continued to have symptoms from limited bladder capacity.

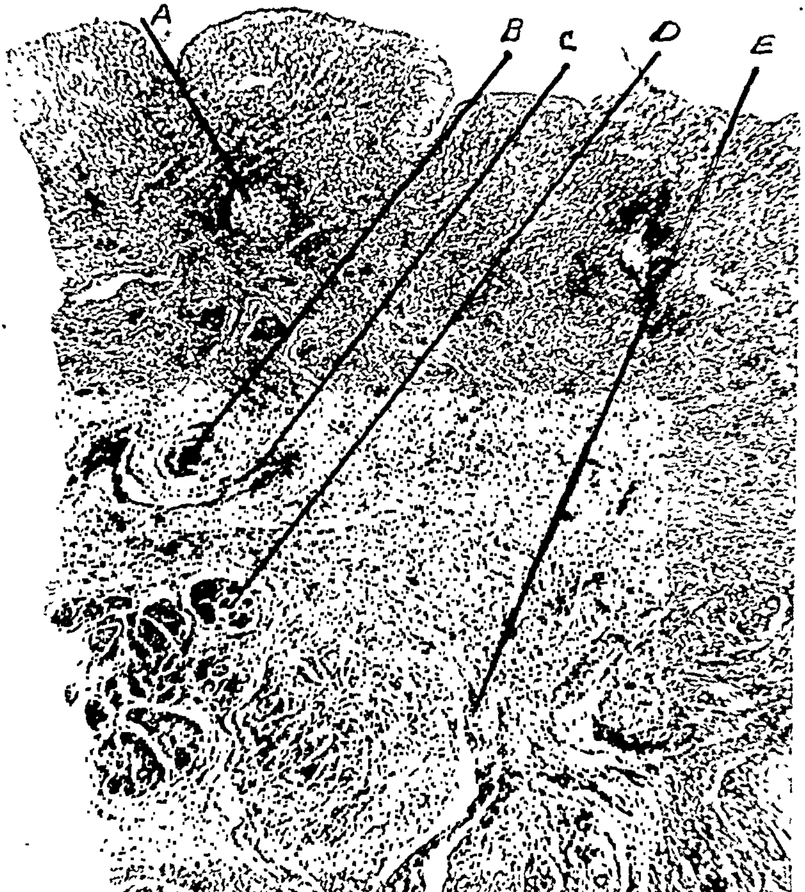


Fig. 2. Section through bladder wall. *A*, Depots of lymphoid cells. *B*, Thickened arteriole. *C*, Enlarged vein. *D*, Muscle bundles. *E*, Increased fibrous tissue in intramuscular septa.

The bladders of 3 women were put to rest by suprapubic cystostomy. None of the women had relief. One subsequently had a bilateral ureterosigmoidostomy and cystectomy for her intractable pain. Another, who had uncontrollable hemorrhages as well as intractable pain, finally had a bilateral uretero-intestinal anastomosis. Although she had lesions on the walls of her bladder, they were most prominent in the base. In fact, when viewed through the cystoscope the bladder base appeared to be filled with myriads of small geysers spurting blood. Fulguration, like cystostomy, had been without effect.

Nesbit advocated anterolateral chordotomy for the intractable pain of refractory interstitial cystitis. This suggestion deserves consideration, for it may be the ultimate procedure of choice. But from my experience in the 2 cases cited, I would recommend ureteral transplantation when either pain or hemorrhage cannot be controlled, at least until end-results from the two procedures can be compared. Since the pain was completely controlled by ureteral transplantation without cystectomy in the second case, perhaps the bladder need not be removed.

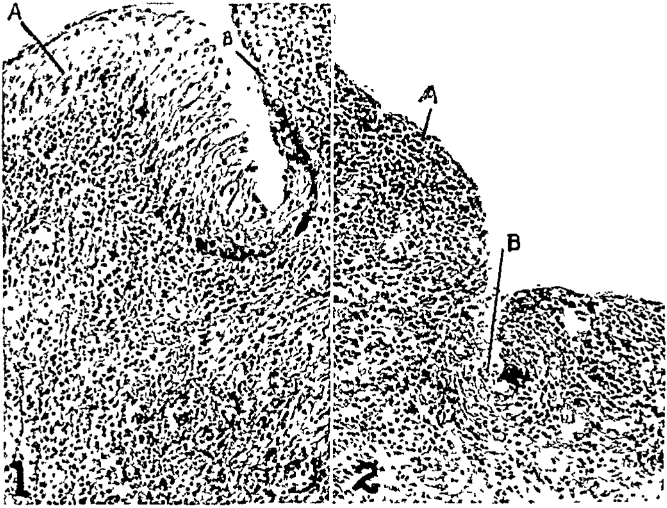


FIG. 3 *1A*, High power field of figure 2, showing varying degrees of mucosal thickness. *A*, Transitional epithelium *B*, Limiting membrane. *2*, High power field of figure 2. *A*, Limiting membrane. *B*, Site of bleeding and break in limiting membrane.

Pathologic studies. Specimens from the lesions of a number of patients were obtained for biopsy. Microsections of these showed essentially the same findings as those from the bladder which had been removed.

Grossly the walls of the extirpated bladder were thickened. The serosal surface presented vascular injection. The perivesical tissues were infiltrated, and there was a definite fixation of the bladder to the surrounding structures.

Microsections (studied with Dr. Frank Menne, pathologist St. Vincent's Hospital, and Dr. Olof Larsell, head of the anatomy department, University of Oregon Medical School) showed a highly vascularized stroma. The subepithelial layer contained monocytes, young fibroblasts, and lymphocytes (fig. 2, *A*). Edema and increased fibrous tissue extended between the muscle bundles. In some areas the intramuscular septa contained an increase of hyaline fibrous connective tissue.

The mucosa varied in thickness (fig. 3, *1 A*). In some areas it was thinned, the thinned portion corresponding to dense subepithelial reaction. In other areas it was denuded so that only the limiting membrane was present. In still other areas even this connective tissue support was broken (fig. 3, *2 B*).

Over the trigone the mucosa was thickened. In the subepethelial tissues there were glands of the type which Emmett and McDonald considered to be similar to those described by Albarran and which they called "glands of subtrigonal type." These subtrigonal glands showed varying degrees of dilatation, some being enormously dilated. Also present in the subtrigonal area were the typical "intestinal type of glands" mentioned by Emmett and McDonald.

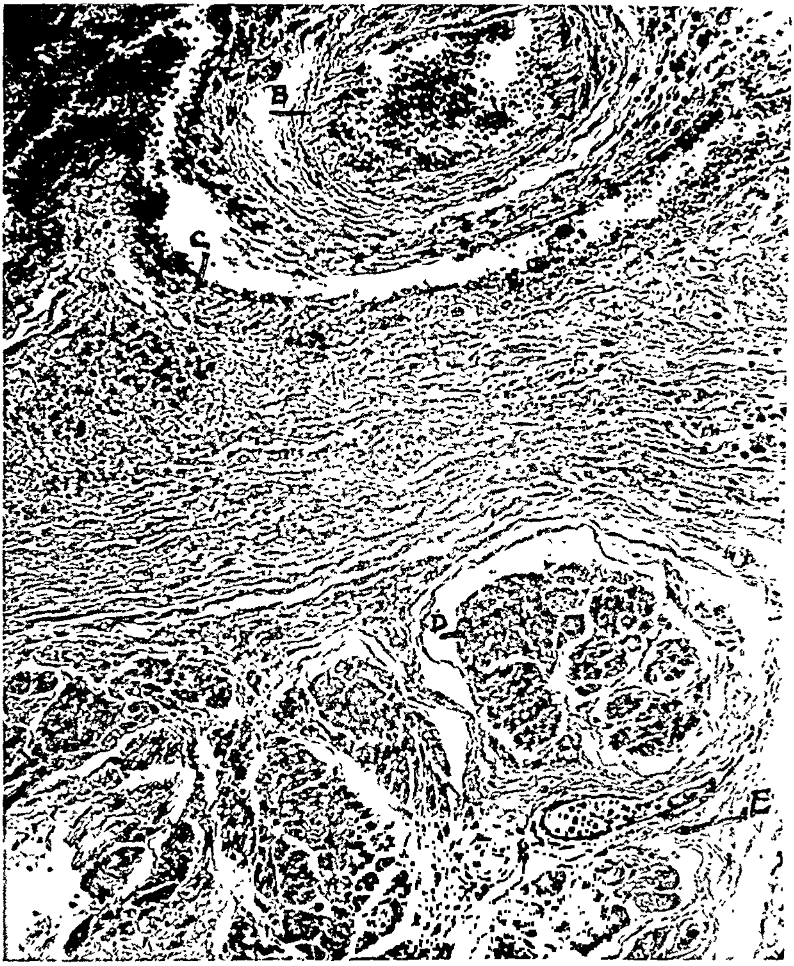


FIG. 4. High power field of figure 2, showing thickened arteriole and dilated, thickened vein. Edema and fibrous connective tissue strands penetrate between muscle bundles.

A few capillaries exhibited evidence of recanalization, suggesting previous embolic phenomena with occlusion. The arterioles had thickened walls and narrow lumens. In some areas the lymph channels were compressed by the surrounding edema and leukocytic infiltration. In others, the cellular infiltration was so dense the lymph channels could not be visualized.

Striking features of the sections were dilatation and engorgement of the various venous structures, from sinusoids (fig. 5) to veins (figs. 2, *C* and 4).

Another striking feature was the abundance of nerve tissue. In some areas the nerves lay just below the margin of subepithelial reaction and in others they penetrated it. There was extensive leukocytic infiltration about and within the nerve sheaths. While the nerves in the deeper structures were intact, those in the area of subepithelial reaction had lost their sheaths and gave the impression of a proliferation of nerve tissue. The intimate relationship between the nerves and the venous sinusoids is shown in figure 5. Langworthy and Hesser have reviewed the innervation of the blood vessels of the bladder.

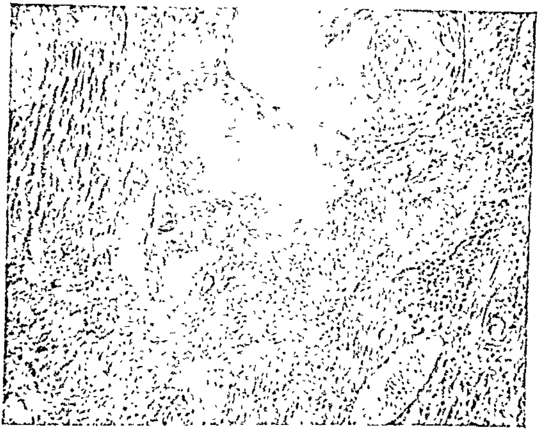


FIG. 5. Masson's stain. *A*, Wall of venous sinusoid composed of single layer of endothelial cells. *B*, Nerve bundle intimately related to wall of venous sinusoid.

Subsequent cystoscopic studies. One man and 34 women had one or more check-up cystoscopies at intervals of a year or longer after the diagnoses of interstitial cystitis had been made. The man, who had had minimal lesions to begin with, showed no lesions on check-up study. Ten women with initial minimal involvement later showed no lesions, but 4 showed persistent lesions. The incidence of persistent lesions was higher in the groups with grade 2 and 3 involvement, 5 and 13 women, respectively.

Follow-up. To evaluate results, a questionnaire was sent to the patients with interstitial cystitis. Only 77 women and 8 men replied. However, 53 women and 1 man had been coming to the Clinic at more or less regular intervals. Thus, a follow-up, varying from 1 to 18 years, was available on 130 women and 9 men.

The data obtained, segregated according to the stage of the lesion, are shown in table 6. Although a few patients reported complete absence of urinary symptoms for several years, and one elderly woman had been symptom-free for more than 10 years, I hesitated to use the term "cured" because of the high incidence of recurrence in this disease. Consequently, "improved" designates patients who had no symptoms or only occasional nocturia, and "partial improvement" designates those who continued to have night frequency from 1 to 2 times. In the "unimproved" group are the patients who had persistent pain of varying degree in addition to continued day and night frequency.

Seventy-five patients, 67 women and 8 men (53.93 per cent) were improved or partially improved. The highest percentage of improvement (62.28 per cent) occurred in the minimal lesion group. The next highest percentage of improvement (44 per cent) was noted in the most advanced lesion group. In the latter are the patients who were older and who had the longest interval between onset of symptoms and diagnosis. It seems, therefore, that in some instances the advanced disease, after persisting for a number of years, finally spends itself spontaneously. The lowest percentage of improvement, as is to be expected, occurred in the grade 2 (active-recurrent) lesion group.

TABLE 6. *End results*

GRADE AND SEX	NO. PTS.	INTERVAL ONSET TO DIAG.*	FOLLOW-UP									NO FOLLOW-UP
			Improved			Partial improvement			Unimproved			
			No. pts.	%	Years*	No. pts.	%	Years*	No. pts.	%	Years*	
		years										
1 F.	138	7½	41	51.3	5½	9	11.3	4¾	30	37.5	4	58
M.	15	5½	5	55.6	6½	3	33.3	3½	1	11.1	6	6
2 F.	37	7½	1	4.0	4½	5	20.0	2	19	76.0	4½	12
M.	4	12½										4
3 F.	29	11½	8	32.0	10½	3	12.0	6¾	14	56.0	6⅓	4
M.												
Total												
F.	204	7½	50	38.5	6	17	13.1	3½	63	48.5	4½	74
M.	19	6½	5	55.6	6½	3	33.3	3½	1	11.1	6	10

* Average number of years.

Five women and 1 man died. None of the deaths were due to the bladder disease.

ANATOMIC AND PHYSIOLOGIC FACTORS

The trigone, which represents the fixed portion of the bladder, is of entodermal origin and is formed by the longitudinal fibers of the ureters as they progress toward the internal sphincter. The medial fibers from each ureter decussate to form Mercier's bar. Drawn taut over the trigone, the mucosa sharply limits distensibility in this area. Trigonal blood supply is the same as that of other portions of the bladder. Trigonal innervation is through the sympathetic nerves.

It has been said that interstitial cystitis cannot involve the trigone because there is practically no subepithelial supportive structure in this area and because, being fixed, no edema can occur there

Microsections of the bladder removed for interstitial cystitis showed considerable supporting tissue under the mucosa of the trigone The blood supply was abundant There was edema, but the degree of edema had been limited by the anatomic structure of the trigone This limitation of edema together with the abundance of the blood supply apparently contribute to the arrest, and possibly the early resolution, of some lesions Support of this hypothesis is the observation that the trigone base area was involved by 50 per cent of the grade 1 lesions but by only 29 per cent of the grade 2 and 6 per cent of the grade 3 lesions Another possible factor favoring trigone-base involvement in women is the mechanical derangement accompanying cystocele Thirty seven women with interstitial cystitis had cystoceles as against 15 in the control group

Trigonal involvement is a cause of bladder irritability, which is expressed by frequency, urgency, and intense pain It is, probably, also associated with stress incontinence In some instances, reflex irritability from the ureters may be another cause of these symptoms

Detrusor muscle involvement is still another cause of bladder irritability This muscle is supplied by the pelvic nerve which has numerous terminal fibers Consequently, when the bladder wall becomes edematous the abundant nerve tissue is involved to the same extent as the subepithelial connective tissue and muscle bundles Anoxemia of the bladder musculature, from impairment of the blood supply, and nerve irritability, from edema and pressure, then combine to cause spasm and pain Since the fibers of the detrusor muscle continue to form the internal sphincter, hyperirritability in one is reflected in the other The work of Heimburger et al suggests a sphincter reflex separate from that controlling the detrusor muscle

ETIOLOGIC FACTORS

Role of infection It is difficult to evaluate the influence of infection in interstitial cystitis On the other hand, the work of many investigators indicates a more than accidental relationship between infection and the bladder disease

From clinical observations, Hunner emphasized foci in the teeth, tonsils, and sinuses as causative factors Rosenow observed localization of virulent streptococci in such vascular organs as the kidneys and lungs Meisser and Bumpus concluded that "submucous ulcer of the bladder" may be due to focal infection harboring streptococci which have a selective affinity for the urinary tract The studies of the Caveltis on the pathogenesis of glomerulonephritis suggest a pathogenesis for interstitial cystitis

Role of circulatory impairment Impaired bladder circulation as a cause of interstitial cystitis is suggested by experimental studies Herbst and his associates, working with dogs, ligated the vessels of the posterior wall and vertex of the bladder and thus produced lesions resembling Hunner ulcers both on cystoscopic and microscopic study

allergy is a perversion of a normal physiologic reaction, the alarm reaction of Selye "

In view of the fact that approximately 15 per cent of the interstitial cystitis patients had allergies of various kinds while only 8 5 per cent of the control patients had such complaints, the occurrence of allergy with interstitial cystitis seems more than coincidental and of sufficient significance to warrant further investigation

Since many patients with interstitial cystitis have a psychogenic makeup, as borne out by this study and those of others, and since, as Selye pointed out, "the general adaptation syndrome is the sum of all nonspecific, systemic reactions of the body which ensue upon long continued exposure to stress," it may be that the nonspecific nature of interstitial cystitis, in part at least, can be explained on the basis of an adaptation disease

DISCUSSION AND CONCLUSIONS

From the foregoing review of various investigations, it is apparent that a number of factors contribute to the pathogenesis of interstitial cystitis Microsections from the bladder of a woman with far advanced interstitial cystitis suggest an etiologic relationship between this disease and the nervous system

Although capillary dilatation was the predominant finding in these sections, there was also thickening of the arterioles, dilatation of the venous structures, and compression of the lymph channels But the most significant finding was the leukocytic infiltration about and within the nerves In some areas it was so extensive that it distorted the normal nerve pattern

In view of these findings, the following questions might well be raised Is the process a vasculitis? Is it the result of venous stasis? Is it due to lymphatic obstruction? After weighing the microscopic evidence of nerve tissue involvement and the clinical evidence suggesting neurogenic stimuli (nervousness, allergies, endocrine disturbances, and some infections), I am inclined to believe that interstitial cystitis is initiated by a neurogenic factor

Whatever the cause of the capillary dilatation seen in this disease, the resultant stasis gives rise to anoxemia Endothelial injury follows It is accompanied by edema of the walls and diapedesis, which is manifested by extravasation of plasma and blood cells into the extra capillary spaces If lymphatic drainage is unimpaired, the congestive process may subside But if lymphatic drainage has been impaired, the stasis and edema progress Two changes then take place First, the overlying mucosa becomes thinned from pressure and microscopic fissures develop The urine bathing these fissures keeps up the irritative process and, finally, produces the lesions of interstitial cystitis Second, the surface erosions then permit exposure of the nerve endings Irritation of these by urine and surrounding inflammation results in local and reflex pain as well as in muscle spasm

That minute, grossly invisible breaks are present in the mucosa is borne out by microsections (figs 3, 2, *B*) Support for the contention that the urine is an irritant is the fact that the 3 women whose bladders were put to rest by cystostomy continued to have pain which in 2 instances became unbearable. But when one bladder was removed and the function of another was interrupted by ureteral transplantation the pain immediately disappeared.

Whether the lesions of interstitial cystitis are graded 1, 2, or 3, as they were here, or in some other manner, is not important. But it is important to be aware of the changing picture of the disease, which is emphasized when an attempt is made to segregate the lesions according to common characteristics. In other words, there is a large element of individual variation in these patients. In my series I was impressed, for example, with the innocent appearance of some lesions, the fulminating character of others, the rapidity with which symptoms can progress, the relentless way in which the disease may persist despite management, and the manner in which a process known to have been intolerable for years ultimately subsides spontaneously.

Although there were many more women than men in this series, there was no appreciable difference in the symptoms nor in the nature of the lesions of the two sexes, except that in the men they did not reach the same degree of severity that they did in the women. The higher incidence in women suggests that the female bladder is rendered more susceptible to interstitial cystitis by its greater tendency to childhood urinary infections; by the trauma of pregnancies; by the mechanical derangement of cystoceles, by the pressure and deformity from fibroids; by the large number of operative procedures on intra-abdominal pelvic organs; by the tissue changes resulting from sodium and water retention associated with the ebb and flow of estrogens during the menstrual cycle; and by the estrogen withdrawal during the menopause with its disturbing physical and psychic manifestations.

In some important respects interstitial cystitis is similar to duodenal ulcer and ulcerative colitis. All three diseases have in common an unknown etiology. And treatment for each is in many cases directed only to control of complications.

Interstitial cystitis is often masked by concurrent diseases which take the patient first to various specialists. Consequently, the responsibility for its earlier diagnosis and better management must be shared by the physician who sees the patient before the urologist.

SUMMARY

An analysis was made of 223 cases of interstitial cystitis (204 women and 19 men). The 3 arbitrary grades for evaluating the lesions were established on the basis of the degree of bladder involvement. Thus, 138 women and 15 men had minimal, or grade 1, lesions; 37 women and 4 men had active, or grade 2, lesions; and 29 women had far advanced, or grade 3, lesions.

There was no difference in the character of the disease in the two sexes, except that in none of the men did the lesions reach the far advanced stage of grade 3. Most of the minimal lesions were found in the trigone-base area, whereas the greatest number of advanced lesions involved either the whole of the bladder or were confined to the dome.

Nineteen patients had no night frequency at the time of the diagnostic cystoscopies. They later developed this symptom.

One patient with interstitial cystitis had a co existing carcinoma of the bladder Ten other cases are cited from the literature

There was a higher incidence of allergies, gallbladder disease, cystoceles, pelvic operations, and some types of foci among the patients with interstitial cystitis than among those in a group selected for comparative study

Treatment of the patients with interstitial cystitis was both general and local The largest percentage of improvement occurred in the minimal lesion group Because of the high incidence of castrates among the women with interstitial cystitis (36 as against 14 in the control group), the need for adequate management of the endocrine factor was stressed Two women had ureteral transplantations for relief of intractable pain One of these women also had a cystectomy

Microsections of the extirpated bladder showed capillary dilatation together with thickening of the arterioles, dilatation of the venous structures, and compression of the lymph channels The most significant finding, however, was nerve involvement, as evidenced by edema and extensive leukocytic infiltration about and within the nerve sheaths

This microscopic evidence of nerve tissue involvement as well as some clinical findings suggest that a neurogenic factor is responsible for the initiation and then the continuation of interstitial cystitis

1216 S W Yamhill St , Portland 5, Ore.

REFERENCES

Adams, A W Refractory ulcerative cystitis Proc Roy Soc Med , 35 434, 1942

Bumpus, H C Jr In discussion on Rusche and Hager

Cavelti, P A , and Else Staehelin Studies on the pathogenesis of glomerulonephritis I Production of autoantibodies to kidney in experimental animals Arch Path , 39 148 1945

Cavelti, P A and Else Staehelin Studies on the pathogenesis of glomerulonephritis, III Clinical and pathologic aspects of the experimental glomerulonephritis produced in rats by means of autoantibodies to kidney Arch Path , 40 163, 1945

Cristol, D S , Greene, L F and Thompson, G J Interstitial cystitis of men, a review of seventy eight cases J A M A , 126 825, 1944

Del Castillo, E B Arconz, J , and Mainini C G Cytological cycle of the urinary sediment and its parallelism with the vaginal cycle J Clin Endocrin 8 76 1948

Eaton, F H Hunner ulcers of the female bladder with review of cases Urol & Cutan Rev , 46 304 1942

Emmett, J L and McDonald, J R Proliferation of glands of the urinary bladder simulating malignant neoplasm J Urol , 48 257, 1942

Engel, W J Interstitial cystitis Cleveland Clin Quart , 6 307, 1939

Fenwick, E H Ulceration of the Bladder Simple, Tuberculous, and Malignant London, J & A Churchill, 1900

Fister, G M Similarity of interstitial cystitis (Hunner ulcer) to lupus erythematosus J Urol , 40 37, 1938

Folsom, A I Hunner's ulcer Texas State J M , 27 718, 1932

Frontz, W A Observations on the pathology, clinical diagnosis and treatment of sub mucous fibrosis (localized cystitis) South M J , 21 899, 1928

Geraghty, J T Infections of bladder with special reference to localized resistant areas of cystitis Surg , Gynec & Obst , 24 655, 1917

Hand, J R Cited by Judd

Hagner, F R Malignancy of bladder occurring in a Hunner ulcer Tr Am A Genito-Urin Surg 30. 197, 1937

Heimburger, R F , Freeman, L W and Wilde, N J Sacral nerve innervation of the human bladder J Neurosurg 5 154 1948

Herbst, R H , Baumrucker, G O and German, K L Elusive ulcer (Hunner) of the bladder with an experimental study of the etiology Am J Surg , 38 152, 1937

Higgins, C C Hunner ulcer of the bladder (review of 100 cases) Ann Int Med , 15 708, 1941

Howard, T. L.: My personal opinions on interstitial cystitis (Hunner's ulcer). J. Urol., **51**: 526, 1944.
Hunner, G. L.: A rare type of bladder ulcer in women; report of cases. Boston M. and S. J., **172**: 660, 1915.
Hunner, G. L.: Elusive ulcer of the bladder. Further notes on a rare type of bladder ulcer, with a report of twenty-five cases. Am. J. Obst., **78**: 374, 1918.
Hunner, G. L.: Intractable bladder symptoms due to urethritis. J. Urol., **4**: 503, 1920.
Hunt, V. C.: Submucous ulcer of the bladder and its surgical treatment. Minnesota Med., **4**: 703, 1921.
Jacobson, E.: You Must Relax. Garden City, N. Y.; Blue Ribbon Books, 1946.
Judd, E. S.: The treatment of carcinoma of the bladder by radical surgical methods. J. A. M. A., **87**: 1620, 1926.
Keene, F. E.: Circumscribed pan-mural ulcerative cystitis, elusive ulcer (Hunner). Ann. Surg., **71**: 479, 1920.
Knisely, M. H., Bloch, E. H., Eliot, T. S. and Warner, L.: Sludged blood. Science, **106**: 431, 1947.
Kreutzmann, H. A. R.: The treatment of Hunner's ulcer with deep x-ray therapy. J. Urol., **46**: 907, 1941.
Langworthy, O. R., and Hesser, F. H.: The innervation of blood vessels as observed in the urinary bladder. Bull. Johns Hopkins Hosp., **67**: 196, 1940.
Learmonth, J. R.: A contribution to the neurophysiology of the urinary bladder in man. Brain, **54**: 147, 1931.
Manning, G. W., Hall, G. E. and Banting, F. G.: Vagus stimulation and the production of myocardial damage. Canad. M. A. J., **37**: 314, 1937.
Meads, A. M.: Hunner ulcer. Urol. & Cutan. Rev., **38**: 631, 1934.
Meisser, J. G. and Bumpus, H. C., Jr.: Focal infections in relation to submucous ulcer of the bladder and to cystitis. J. Urol., **6**: 285, 1921.
Metz, M. H., Lackey, R. W., Wigby, P. E., Small, A. B. and Patterson, C. O.: Peptic ulcer treated by posterior pituitary preparations, clinical and experimental observations. Am. J. Digest. Dis., **7**: 27, 1940.
Miller, H.: Modern concepts of the immunologic basis of clinical allergy. Northwest Med., **47**: 22, 1948.
O'Conor, V. J.: Urologists letters. Second annual vol., June 22, 1935.
Nesbit, R. M.: Anterolateral chordotomy for refractory interstitial cystitis with intractable pain. J. Urol., **57**: 741, 1947.
Peterson, A., and Hager, B. H.: Interstitial cystitis, report of cases. Calif. and West. Med., **31**: 262, 1929.
Powell, T. O.: Studies on the etiology of Hunner ulcer. J. Urol., **53**: 823, 1945.
Rogers, A. L.: The menopause. Portland Clin. Bull., **1**: 62, 1947.
Rogers, A. L.: Personal communication.
Rosenow, E. C.: Elective localization of streptococci. J. A. M. A., **65**: 1687, 1915.
Rusche, C. and Hager, B. H.: Further observations on the development of malignancy in Hunner ulcer. Tr. Am. A. Genito-Urin. Surg., **32**: 203, 1939.
Selye, H.: The general adaptation syndrome and the diseases of adaptation. J. Clin. Endocrin., **6**: 117, 1946.
Skene, A. J. C.: Diseases of the Bladder and Urethra in Women. New York: William Wood & Co., 1887.
Vose, S. N. and Dixey, G. M.: Coincidence of carcinoma of the bladder and interstitial cystitis. J. Urol., **59**: 580, 1948.
Williams, H. L.: The syndrome of physical or intrinsic allergy of the head. II. Ménière's disease (endolymphatic hydrops). Proc. Staff Meet., Mayo Clin., **20**: 373, 1945.
Wilson, R. B. and Mussey, R. D.: Nervous pathways involved in pelvic pain, some anatomic and physiologic aspects. J. A. M. A., **134**: 857, 1947.
Winsbury-White, H. P.: The spread of infection from the uterine cervix to the urinary tract and the ascent of infection from the lower urinary tract to the kidneys. Brit. J. Urol., **5**: 249, 1933.
Ziskin, D. E. and Moulton, R.: A comparison of oral and vaginal epithelial smears. J. Clin. Endocrin., **8**: 146, 1948.

THE JOURNAL OF UROLOGY
Vol 61 No 2 February 1949
Printed in U S A

GIANT HYDRONEPHROSIS REPORT OF A CASE OF INFECTED HYDRONEPHROSIS WITH A CAPACITY OF OVER 9,200 CC[1] [2]

R G WYRENS

The term giant or massive hydronephrosis usually pertains to any containing 1,000 cc or more of urine, or one which almost completely fills the abdominal cavity The incidence of reported cases is not high as is shown by the fact that, in 1939, Stirling was able to collect only 74 cases in a complete review of the world literature However, most experienced urologists have seen a case which qualifies as a giant hydronephrosis Few authentic and even questionable cases have been reported with an estimated or measured capacity of over 9,000 cc, including the old cases of Franck (30 liters), Dumreicher (36 liters) and Glas (30 gallons) referred to by Papin The authenticity of this case by Glas, in particular, has been questioned by most authorities It was alleged to have been found at autopsy in the eighteenth century Sauer stated that the majority reported had a capacity of 2,000 cc to 8,000 cc, and in more recent years the figures have tended to be more conservative

CASE REPORT

Mr G S , aged 62, complained only of vesical obstructive symptoms for the past year Twenty-two years before a vesical calculus was removed by litholapaxy, and he thought that he was suffering from another stone which he wanted crushed and removed transurethrally He denied any other symptoms, stated that he had felt fine and had worked hard every day for the past several years until 1 month ago On direct questioning he admitted that, at this time, he had suffered from a severe, colicky, right upper abdominal pain without radiation which lasted a few days, and for which he sought aid from his local physician He denied having seen any physician before that since the time of the litholapaxy in 1926 On questioning him about his obviously very protuberant abdomen, he was surprised and responded that it had been large for years, but he thought that one usually developed a large abdomen as one increased in age He didn't remember when his abdomen became large, but was sure that it did so gradually

The blood pressure was 138/100, temperature 98 6 F , and pulse 86 beats per minute The examination of the chest and heart was negative His abdomen was greatly distended and a large, firm, multilobulated, nontender mass was palpated filling most of the abdomen, particularly the right flank and abdomen, but extended to fill most of the left abdomen as well, more marked inferiorly (fig 1) Tapping the abdomen elicited a fluid wave, and tympany was percussed only in the left flank There was no costovertebral angle tenderness on either side The prostate gland, per rectum, was enlarged grade 2, and was benign. Two glass voided urine specimens were cloudy of the same density. Calibration of the urethra revealed no stricture, and there were 3 ounces of residual urine.

---

[1] The Joseph F McCarthy prize essay Editor

[2] Read at annual meeting Western Section, American Urological Association, Victoria, British Columbia, April 20, 1948

A chemical examination of a voided urine specimen revealed a slight trace of albumin and no sugar. Microscopically, a centrifuged specimen showed 5 to 10 red blood cells per high power field and a grade 4 pyuria. Gram stain of the urine sediment showed numerous diphtheroids. Serology was negative. There were 12.01 gm. of hemoglobin per 100 cc of blood; 4,130,000 erythrocytes and 6,900 leucocytes per c. mm. of blood. The differential leucocyte count revealed 68 per cent neutrophiles; 27 per cent lymphocytes and 5 per cent monocytes. The blood urea nitrogen was 12.3 mg. per 100 cc of blood; serum calcium 12 mg. and serum phosphorus 2.1 mg. per 100 cc of serum.

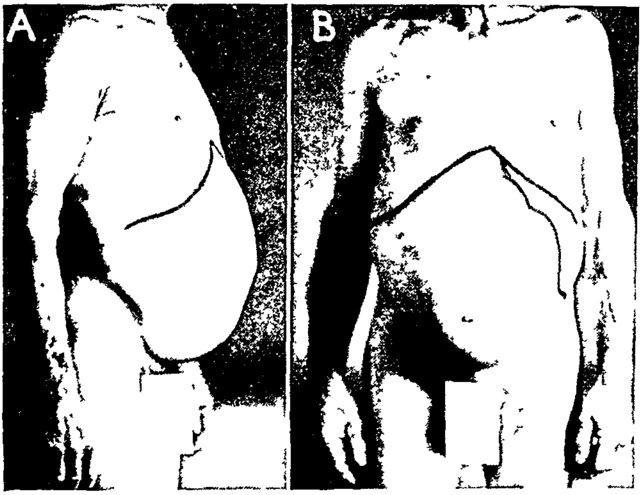


FIG. 1. Preoperative photographs. Left palpable tumor margin and subcostal margin outlined with skin pencil.

A roentgenogram of the chest was negative except for elevation of both sides of the diaphragm. A plain roentgenogram of the kidneys, ureters and bladder revealed a nest of 6 calculi over the right renal area; a nest of numerous stones just above the left iliac crest and another nest of stones over the left sacroiliac synchrondrosis. There was a single calculus 1¼ cm. in diameter over the bladder area and a branched Y-shaped calculus 6½ cm. by 2 cm. in dimensions just to the right and above the left sacroiliac synchrondrosis. A homogeneous density filled all of the abdomen and most of the pelvis suggesting a soft tissue mass. Excretory urograms revealed no function in the right kidney in 2 hours. On the left there was a slight delay in function, and the pelvis and calices were dilated grade one plus. Only the upper third of the ureter was visualized down to, but apparently not including one of the nests of stones previously described (fig. 2, *A*). The ureter was dilated grade 2 plus. There was no medium in the bladder until the 30 minute film. One calculus was included in the bladder.

Cystoscopy showed benign, moderate prostatic hypertrophy with lateral and median lobe hypertrophy, and diffuse chronic cystitis with moderate edema of the base of the bladder. Numerous small cellules and moderate vesical trabeculation were seen. A calculus, 1 to 1½ cm. in diameter, was lying free at the base of the bladder. Both ureters were easily catheterized. The urine flow from the left was brisk and 20 cc clear urine were aspirated from the left renal pelvis, which was normal to microscopic examination. No urine appeared from the right. The renal function, as determined by intravenous indigo carmine, was normal from the left and, of course, none appeared on the right.

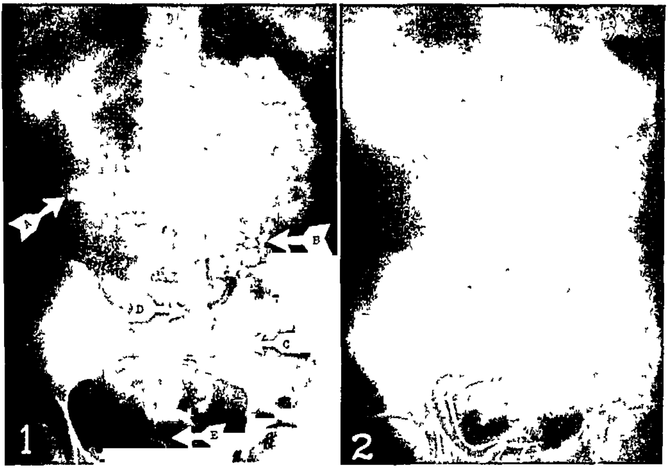


FIG 2 *1*, 20 minute film of preoperative excretory urogram. Note left hydronephrosis. Nest of calculi *A*, *B*, and *C* are in right kidney Two calculi (superimposed) at *D* are in right ureter Vesical calculus at *E* *2*, Preoperative left retrograde pyelogram and right ureterogram Note tortuous right ureter extending to left of midline and including large branched calculi.

A plain roentgenogram of the kidneys, ureters and bladder, with radiopaque catheters in place, showed the left catheter up to the level of the twelfth thoracic vertebra. The right catheter, coiled at the tip, was up to the level of the promontory of the sacrum in the midline, extending up to a branched calculus previously described. All the calculi were excluded from the left kidney and ureter.

Retrograde pyel-oureterograms revealed no dye in the right kidney (fig. 2, *B*). The lower one half of a tortuous right ureter was visualized extending up towards the midline, and the medium extended in it to the branched calculus which was probably included. The left kidney and ureter revealed a hydronephrosis and hydroureter of the upper third of the ureter comparable to the excretory urogram findings. The middle third of the left ureter was not filled and the lower third appeared normal.

With a preoperative diagnosis of a right giant hydronephrosis due to a ureteral calculus, under pontocaine and glucose spinal and sodium pentothal intravenous anesthesia, the patient was subjected to a right nephrectomy and partial ureterectomy. A usual primary, posterolateral right lumbar incision, approximately 10 to 12 inches long, was made; the twelfth rib was not removed. On opening Gerota's fascia, a tremendous, tense, thick-walled cystic mass was encountered. This was pierced with the point of a scalpel and frankly purulent urine, amounting to thin pus, escaped from under great pressure. The aspirator was immediately inserted and the kidney was evacuated of 9,200 cc of this solution. At least another 500 cc escaped collection.

The kidney, a huge, thick, fibrotic shell, was bluntly and sharply dissected from the surrounding retroperitoneal structures and peritoneum. The upper half of the ureter was dissected free and divided just below the obstructing calculi, at the junction of the upper and middle thirds. This kidney tumor extended up and was adherent to the under surface of the whole right diaphragm, extending deep into the pelvis on both sides, and over across the midline well into the left flank. In several small places it was closely adherent to the peritoneum, and one small rent, accidentally made, was promptly closed. The mass was dissected free until only the renal pedicle remained. This was doubly clamped and cut, and the kidney was lifted away, followed by the usual pedicle ligation. After bleeding was completely controlled, 5 gm. of sulfathiazole crystals, several Penrose drains and a large iodoform pack were inserted into the wound. The wound was closed in layers in the usual manner.

Blood loss proved to be moderate. The patient received 1,000 cc of whole blood, one unit of plasma and 750 cc of physiological saline intravenously, during the course of this 2 hour, 15 minutes operation. His systolic blood pressure remained normal during the first hour, and then slowly fell to 85 mm. of mercury by the end of the operation. His pulse increased to 112 beats per minute but always remained of good quality, and the patient showed no other signs of shock.

The pathologist described a collapsed, tremendous hydronephrotic kidney weighing 1,560 gm. and measuring 30 cm. by 15 cm.; the attached ureter was 13 cm. long.

Section of the kidney revealed extreme dilatation of the calyces and pelvis and marked atrophy of the renal parenchyma with a firm, leathery, white, fibrous membrane replacing the renal tissue. In a number of calyces were several loose stones, 5 to 15 mm. in diameter. In the distal end of the attached ureter were two incarcerated stones, each about 3 cm. by 1.7 cm. These completely obstructed the ureter which was adherent to them. Microsections of the cortical kidney tissue revealed that all normal parenchyma was replaced by dense, hyalin, fibrous connective tissue containing scattered infiltrates of many lymphocytes and plasma cells. See figure 3.

Microscopic analysis of the aspirated urine revealed a few red blood cells and innumerable pus cells. The Gram stain revealed Gram negative bacilli, and cultures showed Pseudomonas and Proteus. Analysis of the renal calculi revealed calcium, oxalates and phosphates.

The patient made a remarkably uneventful postoperative recovery following this extensive operation and the highest postoperative temperature reached was 101.4 F.

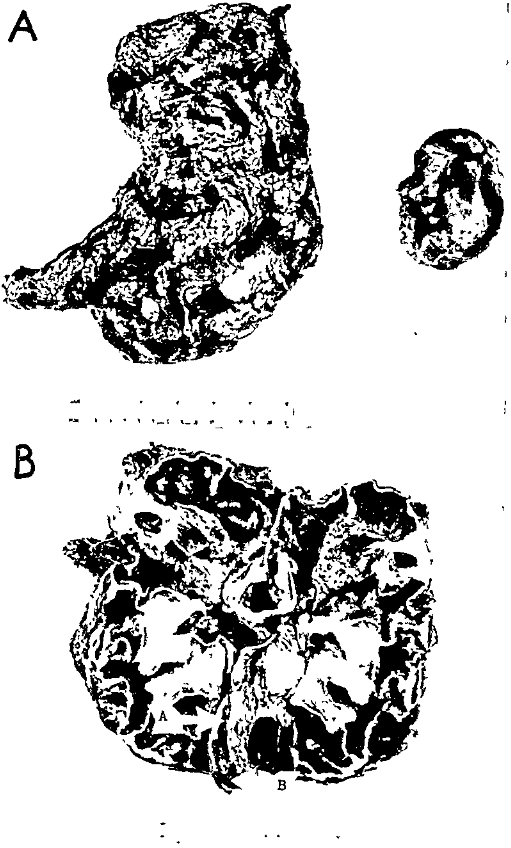


FIG. 3. Specimen removed at operation as compared with normal-sized kidney (upper right). Incarcerated, obstructing ureteral calculi partially shown at *A* and *B*, in sectioned specimen, *B*.

On the seventh day a litholapaxy and transurethral prostatic resection were performed. Seventeen and one half grams of benign prostatic tissue were excised. The patient withstood the procedure very well and his catheter was removed 2 days later.

A mild infection developed in the wound but responded satisfactorily to repeated local applications of sterile, hot wet dressings.

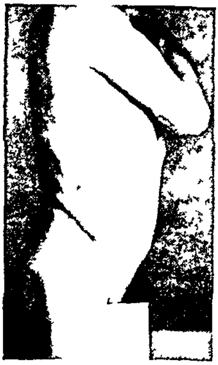


Fig 4 Postoperative photograph of patient. Note nephrectomy scar

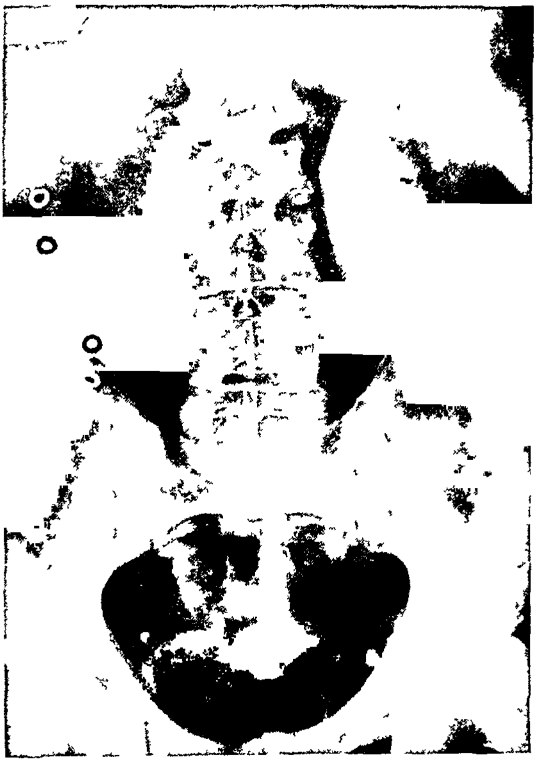


Fig. 5 Fifteen minute film of postoperative excretory urogram. Note absence of left hydronephrosis.

Nineteen days following nephrectomy he was discharged from the hospital. At this time there was a very slight purulent drainage from the posterior angle of his nephrectomy wound (fig. 4). He was voiding a good stream with no nocturia, and there was no residual urine.

Follow-up excretory urograms revealed that the function of the left kidney had improved to normal and there was no evidence of left hydronephrosis (fig. 5).

COMMENT

Several aspects of the case are unusual. In addition to the great size of the hydronephrosis, this patient is one of the oldest to be reported. The presence of this condition in the younger age groups is probably linked up with its more common etiology. As is pointed out by many, the most common causes are congenital factors, either obstructive, adynamic or idiopathic in nature. Of the reported cases, calculus obstruction seemed to be a rare cause.

Stirling mentioned that these huge hydronephroses rarely became infected and this fact accounts for their great size, as early infection tended to produce atrophy rather than hypertrophy. By far the majority of cases reported were sterile. Infection must have been present for a considerable length of time in this case, which is evidenced by the marked fibrotic and chronic inflammatory reaction of the kidney found on pathologic study. The hydronephrosis may have been sterile until it reached its present size, and then became infected. There must have been little or no absorption from this infected kidney at the time I first saw him, as he presented no suggestive symptoms, physical or laboratory findings of a general reaction, except, perhaps, the mild secondary anemia that was present. He must have been well immunized to this particular infection as is evidenced by the little postoperative reaction to the extensive retroperitoneal contamination which was unavoidable at the time of operation.

The majority of these cases produce symptoms referrable to the kidney itself or due to the pressure on the adjacent nerve plexuses or intraperitoneal contents. A few of them, however, produce few or no symptoms as was true with this case. Occasionally, a massive hydronephrosis ruptures, due to slight trauma, which first brings the patient to the doctor. Zimet and Kappel recently reported the first case in which a giant hydronephrosis produced pressure and a hydronephrosis of the opposite side. The same occurred in this case, although no symptoms were produced.

The patient was referred to me with the following diagnoses: myocardial failure with ascites; bilateral nephrolithiasis and ureterolithiasis and a vesical calculus; and a probable right renal neoplasm. The incorrect diagnosis cannot be considered too unusual. In Howze's series of 32 cases the wrong diagnosis was made and laparotomy performed in 11. Of the 26 cases that Stirling reviewed an erroneous diagnosis was made in 7. In more than one reported case the patient had been repeatedly aspirated through the anterior abdominal wall for a suspected ascites. The preoperative urologic roentgenograms are interesting in view of the previous diagnosis of bilateral nephrolithiasis and ureterolithiasis. Most of the calculi present in the right kidney and ureter were located well in the left abdomen and pelvis. As is seen in figure 2, the left ureterectasis extended down to a group of right renal calculi. This may give an untrained observer the impression that the left hydronephrosis was due to obstruction from these calculi in the left ureter.

The question quite naturally arises as to why some of these hydronephroses reach such tremendous sizes. They are usually caused by a partial or intermittent type of obstruction of just the right degree. From the bacteriologic and pathologic evidence, in this case there is no question that the incarcerated ureteral calculi caused a complete obstruction. It is likely that the obstruction was incomplete or intermittent during its formative period.

Many of these enlarged kidneys were surgically approached by the transabdominal route but, in most instances some other intraperitoneal lesion was suspected. The lumbar, extraperitoneal approach with nephrectomy is the preferred, and a preliminary nephrostomy is advocated by some. In the smaller cases, nephrectomy may be performed without first emptying the hydronephrotic sac, but such a procedure would be injudicious in so large one here described.

The question of shock and collapse due to the rapid evacuation of such a large mass of intra-abdominal fluid was considered, but there were no signs of such in my case nor in many others.

Primarily, this operation was performed for the purpose of preventing the progress of the disease to the patient's only functioning kidney. Of secondary importance were the episode of abdominal pain 1 month earlier, danger of rupture of the hydronephrotic sac, the possibility of absorption of toxic products from the pyonephrosis, and the possibility of the vesical calculi being secondary to upper urinary calculi.

SUMMARY

A case is reported of a 62 year old man with an almost asymptomatic, infected calculus pyonephrosis due to a midureteral obstruction from two large incarcerated calculi. The kidney tumor filled most of the abdomen and pelvis and exerted pressure on the left ureter causing a moderate, noninfected left hydronephrosis.

A nephrectomy was performed, extraperitoneally, through a usual posterolateral lumbar incision, after over 9,200 cc of infected, purulent urine were evacuated from the kidney. One week later, a transurethral prostatic resection and litholapaxy were performed.

Following both procedures, his convalescence was essentially uneventful.

1503 Medical Dental Bldg., Seattle 1, Wash.

REFERENCES

Howze, C. P.: Giant hydronephrosis: Report of case. Trans. Am. Assn. Genito-Urin. Surg., **28:** 1–7, 1935.

Papin, E.: Referred to by Wilder, W. O. and Doolittle, L. H.: "Gigantic" hydronephrosis. J. Urol., **34:** 356–358, 1935.

Sauer, H. R.: Massive hydronephrosis: Report of one case. J. Urol., **47:** 416–420, 1942.

Stirling, W. C.: Massive hydronephrosis complicated by hydroureter. J. Urol., **42:** 520–533, 1939.

Zimet, R. R. and Kappel, L.: Giant hydronephrosis as a cause of pyonephrosis in the opposite kidney: Report of a case. J. Urol., **56:** 515–519, 1946.

THE JOURNAL OF UROLOGY
Vol 61 No 2 February 1949
Printed in U S A

CYSTIC DISEASE OF THE KIDNEY DIAGNOSIS AND TREATMENT[1]

CHARLES PIERRE MATHÉ
From the Urological Departments of the Saint Mary's and the Southern Pacific General Hospitals, San Francisco, Calif

The diagnosis and treatment of cystic disease of the kidney often tax the ingenuity of the attending urologist In many cases the clinical examination of the patient presenting the characteristic pyelographic defect will reveal the diagnosis In others the condition is encountered at operation for some other kidney lesion or is discovered at the autopsy table As a rule, polycystic disease is more readily recognized, and in an early case complicated by unilateral destructive kidney disease, nephrectomy may be indicated In patients with polycystic disease we have found complicating hydronephrosis due to torsion of the kidney, which was relieved by conservative surgery, and also massive renal hemorrhage requiring radical operation

This paper is a review of 48 patients, of whom 27 were operated upon for simple renal cysts, solitary or multiple, and 4 for some complication of polycystic disease Our primary purpose is to clarify the surgical treatment, especially of those cysts located in the midportion of the kidney The smaller ones are usually amenable to decapping and cauterization, the large ones and the smaller deep hidden type simulating cancer are best treated by nephrectomy In these centrally located cysts the choice between conservative and radical operation should be based on the size of the cyst, the peculiarities of its location, and the condition of the opposite kidney

ETIOLOGY

It is not the scope of this paper to discuss the etiology of renal cystic disease. In passing, we may state that many writers still adhere to the congenital theory of the early investigators Virchow, and later Caulk, believed that inflammatory sclerosis accompanying nephritis caused occlusion of the uriniferous tubules, resulting in retention cysts Rokitansky felt that they were due to a metamorphosis of the Malpighian bodies Albarran and Imbert, and others, advanced a theory that they arose from remnants of the wolffian body Kampmeier pointed out their frequency in the third and fourth month of fetal life, and stated that they may either degenerate or may grow and expand Hepler, in experimental work on rabbits, proved that to produce a cyst there must be interference with the blood supply as well as occlusion Recently it has been shown that certain peripelvic cysts, in contradistinction to those located in the parenchyma, are lymphangiomatous *in origin*, caused by lymphatic estasia, *with dilatation of* the lymph trunks of the renal pelvis (Henthorne, Scholl, and others) In reviewing our cases of simple cysts we were impressed by the fact that the majority occurred late in life, a fact favoring the theory that cystic disease is often an acquired lesion.

---

[1] Read at annual meeting Western Section, American Urological Association, Victoria, British Columbia, April 21, 1948

SYMPTOMATOLOGY

Symptoms of cystic disease of the kidney may vary considerably. Often the smaller cysts are entirely asymptomatic and are discovered when operating upon the kidney for some other pathological condition. Larger cysts may exert pressure on adjacent organs and give rise to a multiplicity of symptoms referrable to the liver, lungs, gastro-intestinal tract, or cardiovascular system. A complete description of the symptomatology is found in articles by Gutierrez, Llanos, Lowsley and Curtis, and Reaves. In our series we were impressed by the great frequency of microscopic hematuria. The differential diagnosis between a centrally located cyst and a renal tumor in patients with hematuria and a pyelographic defect is often most difficult. In many cases the diagnosis can be made only by operation. In hidden cysts in the midportion of the kidney, nephrectomy and pathological examination of the removed kidney may be necessary to corroborate the diagnosis.

SURGICAL TREATMENT

We are particularly interested in the surgery of polycystic disease and of simple cysts located in the midportion of the kidney. In cases of advanced cystic formation of the kidney, and when the organ is destroyed by a concomitant pathological condition such as sclerosing pyelonephritis, calculous disease, or tuberculosis, nephrectomy is the treatment of choice. In certain cases of polycystic disease and large solitary cysts, puncture and aspiration or marsupialization may be indicated. The management of cysts in either pole of the kidney is well understood, as they are usually amenable to partial resection of the kidney, first successfully accomplished by Tuffier in 1891. Patients with polycystic disease sometimes develop intercurrent disease requiring some sort of surgical intervention, either conservative or radical. Such a patient was Mrs. K. M. (No. 256729) who developed a hydronephrosis secondary to renal torsion. She was relieved from invalidism by decapping, puncturing, and cauterization of numerous cysts of various sizes in the kidney and liver, nephropexy, and sympathectomy. One case of advanced polycystic disease was treated by multiple punctures, and in another nephrectomy was done because of destructive sclerosing calculous pyelonephritis. In 1 patient with advanced bilateral polycystic kidneys, in which a massive exsanguinating hemorrhage occurred in the right kidney, nephrectomy failed to save the patient's life because of insufficient functional renal parenchyma in the remaining kidney. (See figures 1 and 2.)

We are especially interested in clarifying the surgical treatment of cysts located in the midportion of the kidney. These often present the characteristic pyelographic defect of a neoplasm. Pain, hematuria, and palpable tumor may be present in varying degree. If the cyst can be visualized at operation, and is not too large, the free portion can be resected and the interior of the cyst cauterized with nitrate of silver, phenol, or Zenker's solution. We have done this procedure successfully in 4 cases. If the cyst cannot be visualized we believe that the kidney should not be explored by nephrotomy, as this might tend to spread cancer cells if a malignancy should be present. A case in point was Mrs. M. C. (No. 03990). Examination had revealed an enlarged tender left kidney, hematuria, and a pyelographic defect in the upper pole of the left kidney charac-

[illegible] torsion of right polycystic kidney. [illegible]. Patient bedridden because of fre- [illegible] chills and fever. Decapping, puncture and cauterization of cysts of kidney and liver, nephropexy and sympathetectomy relieved patient

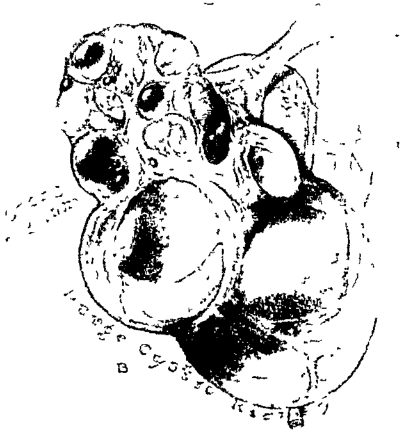


Fig 2 Showing strangulated right polycystic kidney Ptosed polycystic left kidney was not operated on as it caused no symptoms.

teristic of tumor. At operation we found palpable swelling and induration in the upper pole of the kidney, and after consulting with the hospital pathologist,

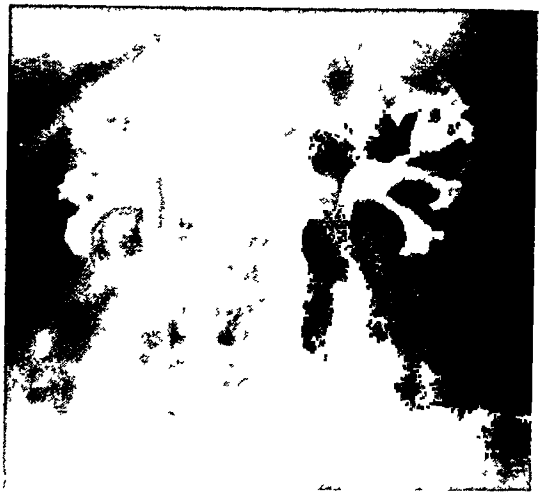


Fig. 3 Retrograde pyelogram showing pyelographic defect in upper midportion of left kidney. At operation indurated tumor was encountered Because of history of hematuria, local swelling and pain, nephrectomy was elected

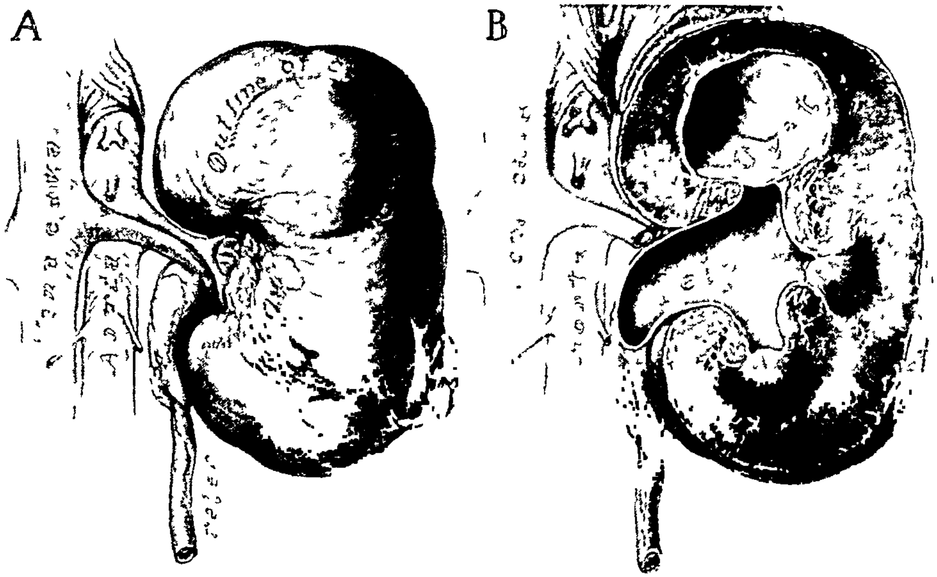


Fig. 4. *A*, left, showing round, indurated mass in mid-upper portion of kidney; pathological examination revealed a cyst containing a polyp *B*, right, sagittal section showing position of cyst in mid-upper portion of kidney exerting pressure on upper major calyx.

a nephrectomy was done. The pathological examination revealed a fairly large cyst in the upper pole containing a polyp. (See figures 3 and 4.)

If the centrally located cyst is of considerable size, nephrectomy is the proper treatment, as an attempt to remove the cyst is usually accompanied by brisk hemorrhage that is likely to necessitate immediate removal of the kidney. We had such a problem in Mr. G. M. (No. 25841). (See figures 5 and 6.) Intravenous and retrograde pyelography revealed a defect in the region of the middle and upper calyces Pain, hematuria, and tumefaction were present At operation a large peripelvic lymphatic cyst was encountered We considered resection of the cyst too hazardous and elected to do a nephrectomy In dealing

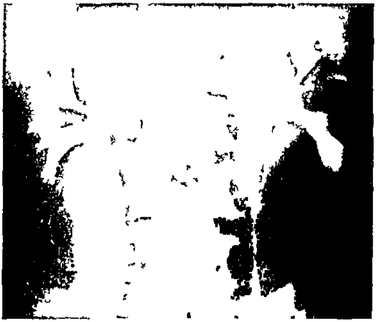


FIG 5 Retrograde pyelogram revealing elongation and narrowing of middle major and minor calyces Intravenous urogram revealed enlargement of kidney in region of pyelographic defect At operation peripelvic lymphatic cyst encountered Nephrectomy

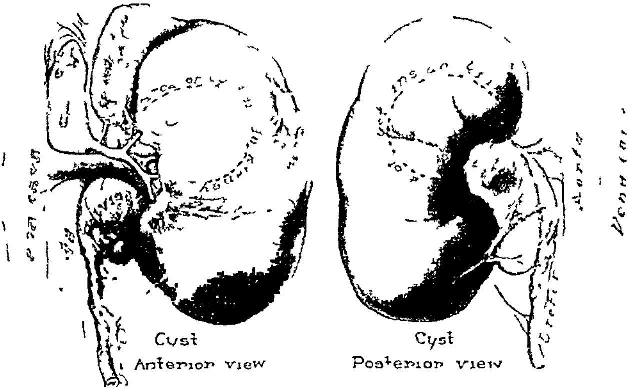


FIG 6 Showing position and size of large peripelvic cyst arising from lymphatic trunks of hilus of kidney

with the large cyst in the midportion of the kidney, not amenable to resection or decapping and cauterization, nephrectomy is indicated, except in those occurring in a solitary kidney, where puncture and cauterization may be the only possible procedure In handling a centrally located hemorrhagic cyst it is usually best to sacrifice the kidney, since 25 per cent of these are accompanied by malignant disease.

ANALYSIS OF CASES

We have operated upon 31 patients for cystic disease of the kidneys at St. Mary's Hospital and the Southern Pacific General Hospital from January 1930 to January 1948. Eight cases of simple renal cyst, in which the diagnosis was not confirmed by operation, 2 solitary cysts found at autopsy, and 7 cases of unoperated polycystic disease are not included. There were 17 polar cysts, 12 in the upper and 5 in the lower pole. Partial resection of the kidney, including the polar cyst, was carried out in 6 cases. In three of these it was possible to ligate the nutrient artery prior to resection. Decapping and cauterization was done in 11 cases, and puncture alone in 1. In this patient resection of the cyst was planned, but the patient went into shock on the table and we were forced to resort to rapid evacuation by puncture. Eight cases presenting larger cysts were diagnosed before operation, and 9 were discovered while intervening for renal ptosis, stone, or hydronephrosis. In 1 patient with a hemorrhagic cyst, the kidney was removed.

TABLE 1.—*Summary of operative procedures*

1. *For single or multiple simple polar cysts*	
Partial resection of kidney including cyst	6
Decapping and cauterization	
Single cyst	11
Multiple cysts (usually two)	4
Total	21
2. For cyst in the midportion of the kidney	
Decapping and cauterization	3
Nephrectomy	3
Total	6
3. For polycystic disease	
Multiple decapping and cauterization	1
Same plus nephropexy and sympathectomy	1
Nephrectomy	
For destructive calculus disease	1
For massive hemorrhage	1
Total	4
4. Concomitant procedures	
Nephropexy and sympathectomy	8
Same with ligation of aberrant vessel	2
Pyelolithotomy	3
Drainage of cortical abscess	1
Total	14

The cysts involving the midportion of the kidney presented the greater problem both in diagnosis and treatment In 2 of them we could not distinguish the cyst from a tumor either before operation or at the time of surgery In both of these the presence of hematuria and of a constant pressure defect in the pyelogram led us to decide on nephrectomy after consultation with the hospital pathologist We also removed the kidney in a patient in whom it was impossible to remove a large centrally located cyst without danger of grave hemorrhage We chose nephrectomy rather than mere puncture because of the possibility of complicating malignancy In two patients presenting smaller cysts exerting definite pressure on the renal circulation, decapping and cauterization were done One of these patients was relieved from renal hypertension, the other subsequently developed tuberculosis in the kidney requiring nephrectomy In 1 case decapping and cauterization were done at the time of a nephrolithotomy

Four patients presented cysts of the upper and lower pole, these were of unequal size and were treated by decapping and cauterization

Concomitant operations consisted of nephropexy and sympathectomy in 10 cases, pyelolithotomy in 3, and 1 drainage of a cortical abscess

Seven patients had polycystic disease and were referred for medical care, 4 were treated by either conservative or radical surgery, and 2 were discovered at autopsy

SUMMARY

A review is presented of 48 patients with cystic disease of the kidney found at St Mary's Hospital and the Southern Pacific General Hospital from January 1930 to January 1948 Thirty-one were subjected to operation, 2 were discovered at autopsy, and 15 were diagnosed by clinical examination

Partial resection of the kidney is the treatment of choice for cysts located in either pole and was successfully carried out in 6 cases Decapping and cauterization was employed in 20 cases and nephrectomy in 5

Smaller cysts located in the midportion of the kidney are best treated by decapping and cauterization In the larger cysts and the smaller hidden type simulating cancer it is best to do a nephrectomy if the other kidney is normal

Nephrectomy is indicated in the earlier cases of polycystic disease complicated by unilateral destructive lesions of the kidney such as sclerosing pyelonephritis, stone formation, or tuberculosis

One patient is described presenting polycystic disease with intercurrent disease consisting of hydronephrosis secondary to renal torsion, who was relieved from invalidism by decapping, puncture, and cauterization of the cysts in the kidney and liver, together with nephropexy and sympathectomy.

450 Sutter St , San Francisco, Calif

REFERENCES

ALBARRAN, J AND IMBERT, J Les tumeurs du rein Paris, Masson & Cie , 1903, p 589

CAULK, J R Obstructive calcareous papillitis, retention cysts of kidney Tr Am A Genito Urin Surg 7 228-255 1912

GUTIERREZ, R.: Large solitary cyst of the kidney. Arch. Surg., **44:** 279–318, 1942.
HENTHORNE, J. C.: Peripelvic lymphatic cysts of the kidney. Am. J. Clin. Path., **8:** 28–38 1938.
HEPLER, A. B.: Solitary cyst of the kidney. Surg. Gynec. & Obst., **50:** 668–687, 1930.
KAMPMEIER, O. F.: A hitherto recognized mode of origin of congenital renal cyst. Surg. Gynec. & Obst., **36:** 208–216, 1923.
LLANOS, M. A.: Riñón poliquístico. Rev. Argentina de Urol., Nos. 11 and 12, 1937.
LOWSLEY, O. S. AND CURTIS, M. S.: The surgical aspects of cystic disease of the kidney. J. A. M. A., **137:** 1112–1119, 1945.
REAVES, J. U.: Polycystic kidney disease—its surgical management. South. Surg., **11:** 254–289, 1942.
VON ROKITANSKY, C.: A manual of pathologic anatomy, translated by E. Sieverking. Philadelphia: Blanchard & Lea, 1855, vol. 2.
SCHOLL, A. J.: Peripelvic lymphatic cysts of the kidney. J. A. M. A., **136:** 4–7, 1948.
TUFFIER, M.: De l'ablation par dissection des grands kystes séreux du rein. Arch. gén. de méd., **2:** 5–13, 1891.
VIRCHOW, R.: Die krankhaften geschwulste, Berlin: A. Hirschwald, 1863–1867, vols. 1 to 3.

THE JOURNAL OF UROLOGY
Vol 61 No 2 February 1949
Printed in U S A

TRUE RIGHT SUPERNUMERARY KIDNEY DIAGNOSED PREOPERATIVELY[1]

CHARLES MONTGOMERY STEWART
From the Department of Urology, Moore White Foundation, Los Angeles, Calif

Conclusive preoperative diagnosis of true supernumerary kidney has been established only 3 times in the world's literature since 1677 The fourth case of the rarest of renal anomalies diagnosed before operation is hereby recorded This report increases to 49 the total number of cases on written record diagnosed either pre- or postoperatively

To this author's knowledge, the last case in the literature, reported by Carlson in 1946, increased the previously recorded total number of cases to 48 The diagnosis in this instance was not suspected preoperatively Carlson completely reviewed the general anatomical characteristics, pathological variations, diagnosis and discussed the recommended treatment of this unusual condition These aspects need not be repeated at this time

Bacon reported the forty-seventh case in a paper read at the 1946 meeting of the Western Section of the American Urological Association The embryonic developmental deviations resulting in this rare renal abnormality were recalled in such accurate detail by Bacon that a review of the causes of this anomaly of the excretory ducts would be unnecessarily repetitious

This case fulfills the requirements of Geisinger's description, 'that the supernumerary organ must be a distinct, encapsulated, large or small parenchymatous mass topographically related to the usual kidney by a loose cellular attachment at most and often by no attachment whatsoever " No attachment was demonstrated to this supernumerary kidney at the time of the surgical exploration and removal

CASE REPORT

W R A , No 89053, a man aged 59, was referred for examination by an otolaryngologist who suspected 'a possible chronic prostatitis " His chief complaint was recurrent attacks of lower abdominal midline pain with onset usually following lifting type of exertion, or when straining during bowel movements The pain was sharp in character with radiation into the pelvis, "just inside the rectum " Distress lasted 5 to 10 minutes A feeling of marked nausea followed the onset There was no vomiting Bowel movements afforded no relief The pain was relieved by lying down Attacks occurred 4 to 6 times a year The history was otherwise negative except for nocturia one time

The physical examination was essentially negative except for well healed left herniorrhaphy scar The blood pressure was 124/78 Analysis of the urine specimen was negative except for 40 to 50 red blood cells found per high power field centrifuged. Voided second glass specimens of urine were checked on several occasions and an intermittent microscopic hematuria was noted. The prostate was grade 1 in size, soft, moderately tender, movable, benign to digital examination. The prostatic fluid contained 12 to 15 pus cells per high power field.

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, B C , April 20, 1948

A plain x-ray of the abdomen was negative. The right renal outline was slightly smaller and lying higher than that of the left kidney.

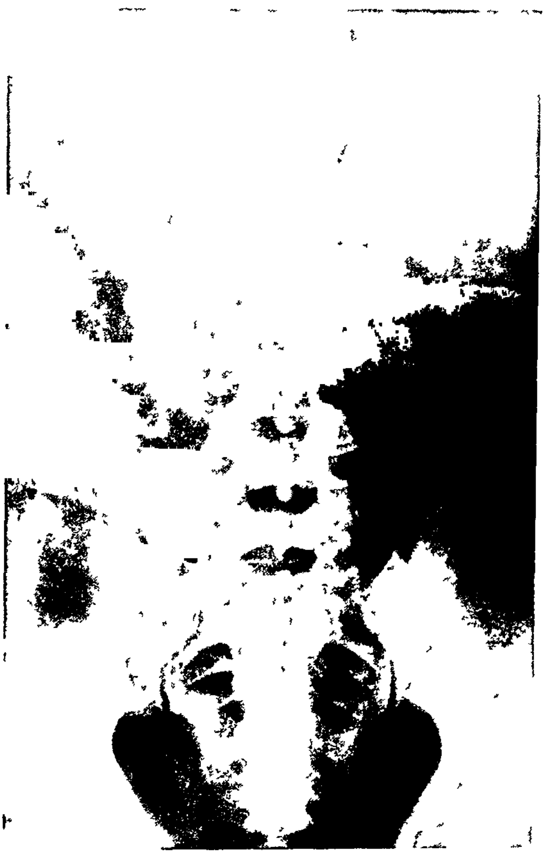


FIG. 1. Intravenous urogram, 5 minute film, showing small, high-lying right kidney. Normal left kidney outline.

Blood examination: Color index 93; hemoglobin 100 per cent; red blood cells 6,060,000; white blood cells 6,100; differential: normal. Sedimentation rate: 5 mm. The phenolsulphonphthalein test showed a 6 minutes' appearance time of dye per urethral catheter. The catheter was removed and a voided specimen collected in 1 hour revealed 55 per cent dye excretion.

The second hour specimen revealed 40 per cent dye excretion.

Intravenous urograms on February 23, 1948 revealed a normal appearance time and concentration of dye on both the right and left sides. The left pyelogram showed no gross abnormality. The right pyelogram revealed rudimentary type of pelvis and calyces. The right kidney outline was smaller than normal and lying higher than normal. There was no evidence of ureteral dilatation, and drainage was adequate in the upright position, after release of compression. See figure 1.

Because of, 1) the rudimentary pyelographic outline of the high-lying right kidney, 2) the small right renal shadow, 3) the patient's complaint of recurrent lower abdominal midline pain and 4) the intermittent microscopic hematuria, the possibility of a right supernumerary kidney was considered.

Cystoscopy under local anesthesia was done at the hospital on February 26. A 24 F. McCarthy panendoscope was passed to the bladder easily. The bladder capacity and bladder mucosa were normal. Inspection of the bladder and bladder neck was accomplished by the fore-oblique, right angle and retrograde lens systems. The left ureteral orifice was normal in position and appearance and showed a clear, active, forceful jet. On the right side, two normal appearing ureteral orifices were noted. The lower right orifice closest to the middle trigone area showed a clear, active, forceful jet. No jet was noted from the upper right orifice. Indigo carmine appeared on the left and from the lower right orifice in 5 minutes, in good concentration. No dye appeared from the upper right orifice in 10 minutes. A 5 W. ureteral catheter was passed easily through the lower right orifice to 30 cm. and active drips of urine were obtained. A 5 W. ureteral catheter was passed through the upper right orifice to 25 cm., where obstruction was noted and about 8 cc of grossly clear urine dripped from the catheter. The drips suddenly stopped and unfortunately were not collected. An x-ray with the two right ureteral catheters in place revealed the upper catheter in a normal position and the lower catheter coiled in the area of the upper right sacroiliac region close to the spine. The tip of this catheter extended several centimeters up beyond the catheter coil. See figure 2, *A*.

Retrograde pyelograms demonstrated the previously reported upper right renal outline. The lower right pyelogram revealed the dilated pelvis and calyces of a separate kidney, located to the right of the spine, just above the right sacroiliac articulation. Several pyelograms were taken as the catheter was withdrawn from the lower right kidney. A pyelo-ureterogram was taken in the upright position. See figure 2, *B* and *C*. Unfortunately, after withdrawing the catheter, an upright film for dye retention was not taken because of the patient's persistent complaint of discomfort.

On March 1, under low spinal anesthesia, cystoscopy was again performed and catheters were passed into all 3 ureters (fig. 3). Phenolsulphonphthalein appeared from the upper right kidney in 5 minutes and from the left kidney in 6½ minutes. Specimens collected for 15 minutes showed 6 per cent dye excretion from the right upper kidney, 8 per cent dye excretion from the left kidney. Irrigation of the supernumerary kidney was done at regular intervals and a very faint appearance of dye was noted in 18 minutes in the irrigation fluid. Cultures from all 3 kidneys showed no growth after 48 hours.

Surgical exploration was performed March 3 under spinal anesthesia.

A transverse incision was made in the right lower quadrant just below the level of the umbilicus. The fascia and peritoneum were opened in the same plane. The posterior parietal peritoneum was incised and the supernumerary kidney readily exposed and mobilized. Both right ureters were identified, care being exercised to preserve the ureter to the right upper kidney. A supernumerary kidney measuring 6 to 7 cm. in length was found on the right side lying in the groove between the psoas muscle and the vertebral bodies in approximately the area of the right sacroiliac articulation. The kidney was composed of markedly dilated calyces and pelvis with very little parenchymal tissue. The upper right kidney and left kidney were palpated and found to be normal except that the right kidney was about one-third smaller than normal. The supernumerary kidney was removed following division and ligation of 3 separate vascular pedicles, one extending from the superior pole to the mid-abdominal aorta and vena cava, another to the lower abdominal aorta and vena cava and the third extended inferiorly to the right external iliac artery and vein. The ureter was divided and ligated and hemostasis secured. The posterior parietal peritoneum was allowed to drop back into normal position. The wound was closed without drainage using No. 0 chromic, continuous suture for the peritoneum and No. 30 stainless steel wire, interrupted, for the fasciae and continuous wire sutures for the subcutaneous tissues and skin. A 500 cc whole blood transfusion was given during operation. The procedure lasted approximately 65 minutes. The patient left the table in excellent condition.

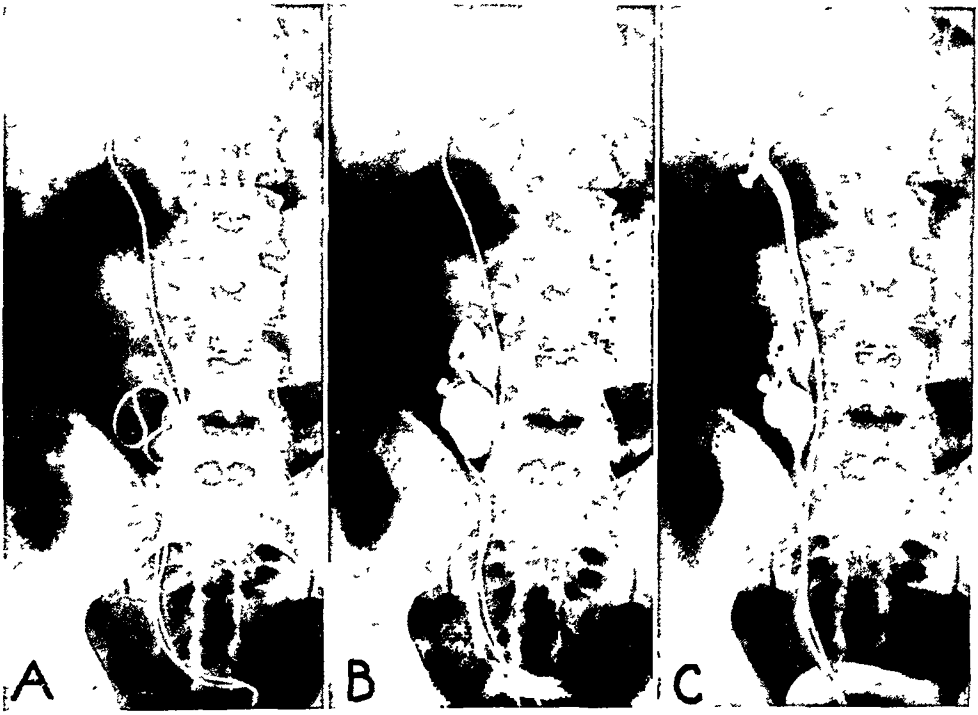


FIG. 2. *A*, left, retrograde kidney study. Plain film on ureteral catheters; 1 catheter in upper right kidney, second catheter coiled in pelvis of lower right supernumerary kidney. *B*, middle, contrast medium injected into lower right kidney in various concentrations as catheter was slowly withdrawn. *C*, right, retrograde pyelograms of upper right kidney and lower right supernumerary kidney.

The gross specimen consisted of a kidney which together with the pelvis measured approximately 7 cm. in its greatest dimension (fig. 4). The pelvis was dilated and largely extrarenal The mucosa of the pelvis showed many areas of recent hemorrhage. The pelvis joined with several irregular dilated calyces which are distended with thin blood tinged fluid. There was no evidence of any discrete tumor mass. The gross architecture of the kidney appeared to be quite well preserved.

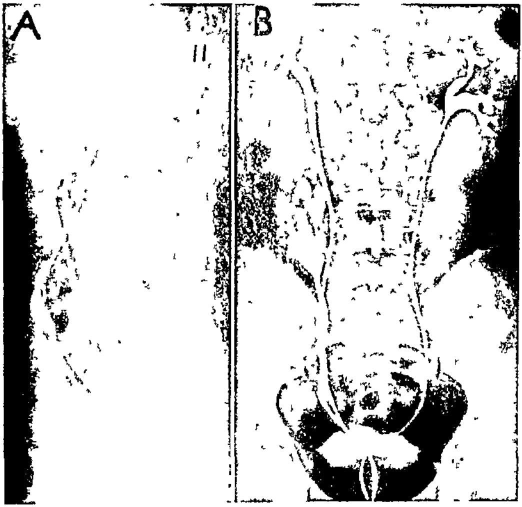


FIG 3. *A*, left, retrograde pyelogram of 3 kidneys, lateral view *B*, right, retrograde pyelogram of 3 kidneys, supine

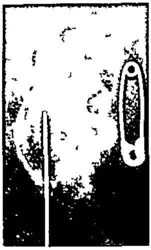


FIG 4. Surgical specimen injected with air

Histological examination of sections taken through various portions of the pelvis showed that the pelvic mucosa was intact and the submucosa showed a few small round cells and many areas of recent hemorrhage. Sections through the remainder of the kidney showed areas of interstitial fibrosis in the tips of the pyramids. The glomeruli showed subintimal hyalin fibrous thickening of their capillaries. The tubules showed no significant abnormality. The small arteries showed slight hyaline intimal thickening. There was no evidence of malignancy. Diagnosis: Hydronephrosis of supernumerary kidney.

The postoperative course was uneventful. The wire sutures were removed on the seventh day. The patient was discharged on the tenth day.

SUMMARY

The fourth case of true supernumerary kidney diagnosed preoperatively is reported, and increases to 49 the total number of cases on record. The operation consisted of transperitoneal removal of the anomalous kidney through a transverse abdominal incision. The postoperative course was uneventful. The patient has had no recurrence of symptoms to date.

511 S. Bonnie Brae, Los Angeles, Calif.

REFERENCES

Bacon, S. K.: Large hydronephrosis of a true supernumerary kidney. J. Urol., **57**: 459, 1947. Also Trans. Western Section A.U.A., **13**: 18–25, 1946.

Carlson, H. E.: Supernumerary kidney as a cause of uretero-pelvic obstruction. J. Urol., **56**: 179–182, 1946.

Exley, N. and Hotchkiss, W. S.: Supernumerary kidney with clear cell carcinoma. J. Urol., **56**: 569, 1944.

Geisinger, J. F.: Supernumerary kidney. J. Urol., **38**: 331–356, 1937.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

CROSSED UNFUSED RENAL ECTOPIA WITH TUMOR[1]

HARRY P. LEE

Crossed, unfused renal ectopia, a congenital condition in which a kidney is transposed to the side of the body opposite its normal location but remains unattached to its normally placed mate, is a rare anomaly. Of all cases of crossed renal ectopia, it is estimated that only 1 in 10 is unfused. No one has as yet satisfactorily explained the embryology by which the condition occurs. About half of the cases have been found in cadavers or at autopsy, evidently having had no symptoms during life. The others have been discovered as abnormal abdominal masses or have developed pathological conditions which in turn have led to urological investigation. Nonunion of the kidneys in the past has been confirmed by autopsy or by surgery. However, with better x-ray techniques, resulting in much better visualization of the kidney shadows, I believe that one may at times make the diagnosis by pyelogram alone, especially in those cases in which the normal kidney occupies a normal position and is normal in all respects, with well demonstrated renal outline, and the abnormal kidney lies far enough away so that it is evident that fusion has not occurred. Attempts also have been made to demonstrate nonfusion by pyelography or by fluoroscopy with the patient in various positions in an effort to show separation of the two kidney shadows or to show that the kidneys lie in different planes. Where the kidneys are close together these methods do not seem to be conclusive.

In crossed renal ectopia, either fused or unfused, the ureters will arise from their normal positions in the bladder, the ureter to the crossed kidney crossing over the midline to the opposite side of the body to enter the misplaced kidney pelvis. A unilateral ectopic kidney lying in the true pelvis in front of the sacrum has a portion of its cortex and pelvis lying on each side of the midline, and at times the catheter will be passed up the short ureter and far into the kidney pelvis, thus crossing the midline. This, however, does not mean that the ureter crosses the midline and the kidney, in my estimation, is still an unilateral uncrossed ectopia.

For an excellent discussion of the embryology, incidence and surgery of these kidneys, reference is made to the paper by Mayers.

Alcock, in 1926, reported 1 case of crossed unfused renal ectopia and reviewed the literature, tabulating 17 cases. In 1936, Mayers, reporting a case, again reviewed the literature, adding 6 cases to Alcock's tabulation, including 1 case that Alcock had rejected (Sutherland and Edington) and leaving out 3 cases that Alcock has accepted (Meyer, Plummer, Herbst), a total of 20 cases. He believed that since Sutherland and Edington's case, reported in 1898, had been included in the tabulation of Papin and Palozolli, it should be given the benefit of the doubt. Alcock, after careful study, stated that the case "is not of the crossed type." Since it is doubtful at best, I have not included this case. Meyer's their capillaries. The tubules showed no significant abnormality. The small arteries showed slight hyaline intimal thickening. There was no evidence of malignancy. Diagnosis: Hydronephrosis of supernumerary kidney.

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, B. C., Canada, April 19, 1948.

The postoperative course was uneventful. The wire sutures were removed on the seventh day. The patient was discharged on the tenth day.

SUMMARY

The fourth case of true supernumerary kidney diagnosed preoperatively is reported, and increases to 49 the total number of cases on record. The operation consisted of transperitoneal removal of the anomalous kidney through a transverse abdominal incision. The postoperative course was uneventful. The patient has had no recurrence of symptoms to date.

511 S. Bonnie Brae, Los Angeles, Calif.

REFERENCES

Bacon, S. K.: Large hydronephrosis of a true supernumerary kidney. J. Urol., **57**: 459, 1947. Also Trans. Western Section A.U.A., **13**: 18–25, 1946.

Carlson, H. E.: Supernumerary kidney as a cause of uretero-pelvic obstruction. J. Urol., **56**: 179–182, 1946.

Exley, N. and Hotchkiss, W. S.: Supernumerary kidney with clear cell carcinoma. J. Urol., **56**: 569, 1944.

Geisinger, J. F.: Supernumerary kidney. J. Urol., **38**: 331–356, 1937.

attached to the left kidney However, in his illustrations, it seems that both kidneys shifted and retained their approximate positions relative to each other and one cannot be certain that they are not fused

Culp (1944) reported 6 cases of crossed renal ectopia His sixth case shows by pyelogram that the left crossed kidney is far below the normally placed right kidney and could not be fused

Nation (1945) in a study of 23 cases of renal ectopia, lists 1 case (case 3) proved at autopsy

Resnick and Clark (1946) reported a case of bilateral ectopia, the right kidney low near the brim of the bony pelvis, the left kidney crossed and lying under the right They state that by fluoroscopy a difference in the planes of the two kidneys was apparent But there is no conclusive evidence that the kidneys were not fused

To this tabulation I wish to add another case, substantiated by pyelography and surgery, and the third case to be reported in which tumor was found Including this case, I can tabulate a total of 29 cases of crossed unfused renal ectopia

CASE REPORT

G E, a married white woman, aged 41, was seen May 28, 1938, complaining of severe pain in the buttocks, extending down the posterior aspect of the thighs to the knees In November 1937 she had had severe chills, headaches and the onset of the pain The pain had become increasingly severe and constant For the past 4 or 5 years she had had urinary frequency, without dysuria or hematuria, which had gradually increased until she was voiding about every hour day and night For 3 or 4 years she had been conscious of a mass in the lower left abdomen which would increase and decrease in size At times the mass had been somewhat tender, never very painful, but when the mass was large the pain in the buttocks and thighs was increased At times she would have much gaseous abdominal distention At no time had she ever passed a large amount of urine with simultaneous decrease in the size of the mass

On physical examination the patient appeared tired and ill Her general development, head, neck and all reflexes were normal The blood pressure was 130/80 Neither kidney was palpable and there was no apparent enlargement of liver or spleen There was a midline suprapubic scar with diastasis of the recti muscles and several small herniations In the depths of the scar one could feel a hard, round, tumor mass, about the size of a large fist, lying to the left of the midline, tender and slightly movable On vaginal examination the cervix looked and felt normal but the patient was so tender and nervous that a good examination of the mass was not accomplished and rectal examination was also unsatisfactory The catheterized bladder urine was very turbid, with albumin 2 plus, a few red blood cells, many pus cells, and the stain of the centrifuged sediment showed many small cocci

On cystoscopy the bladder capacity and force were normal The bladder mucosa was moderately and uniformly reddened The ureteral orifices were

TABLE 1. *Crossed unfused renal ectopia*

AUTHOR	DATE	KIDNEY CROSSED	COMPLICATING PATHOLOY	POSITION OF CROSSED TO NORMAL	SEX	DIAGNOSIS MADE ON
1. Rokitansky	1861	Left	None	Under	Female	Cadaver
2. Weisbach	1867	Left	None	Under	Male	Autopsy
3. Brigidi	1880	Left	None	Under	Male	Autopsy
4. Graser	1895	Left	Pyonephrosis in crossed kidney	Under	Male	Operation and autopsy
5. Schutz	1897	Right	None	Under	Female	Autopsy
6. Kohler	1900	Left	Chronic nephritis	Under	Female	Autopsy
7. Schumacher	1903	Left	None	Under	Female	Autopsy
8. Ghosal	1905	Left	None	Over	Female	Autopsy
9. Heiner	1908	Left	None	Under	Male	Autopsy
10. Plummer	1910	Left	Not mentioned	Under	Male	Surgery
11. Bugbee and Losee	1919	Left	Pyelitis in crossed	Under	Female	Pyelogram
12. Bugbee and Losee	1919	Both	Tuberculosis in right; pyelonephritis in left		Female	Autopsy
13. Huffman	1924	Left	None	Under	Male	Cadaver
14. Beer	1925	Left	Calculus pyonephrosis of crossed	Under	Male	Pyelogram and surgery
15. Alcock	1926	Left	Calculus pyonephrosis in crossed	Under	Male	Pyelogram and surgery
16. Campbell	1930	Left	Hypoplasia of crossed	Under	Male	Autopsy
17. Wear	1930	Left	Hydronephrosis in crossed	Under	Female	Surgery
18. Sigal	1934	Left	None	Under	Male	Surgery
19. Howard	1935	Right	Hydronephrosis in crossed	Under	Male	Surgery
20. Mayers	1936	Left	Calculi in uncrossed pyelitis in both	Under	Male	Pyelogram and surgery
21. Beer and Ferber	1937	Left	Hydronephrosis and stones in crossed	Under	Male	Pyelogram and surgery
22. Beer and Ferber	1937	Right	None	Under	Female	Autopsy
23. Patch	1937	Left	Adenocarcinoma in crossed	Under	Male	Surgery
24. Harris	1939	Left	None	Under	Male	Pyelogram
25. Langworthy and Drexler	1942	Right	Adenocarcinoma in crossed	Under	Male	Surgery
26. Zide and Maher	1943	Right	None	Under	Male	Pyelogram
27. Culp	1944	Left	None	Under	Male	Pyelogram
28. Nation	1945	Right	None	Under	Male	Autopsy
29. Lee	1948	Right	Squamous celled carcinoma in crossed	Under	Female	Pyelogram and surgery

Left kidney crossed	21	Male.......	19	Autopsy or cadaver....	13
Right kidney crossed....	7	Female....	10	Surgery................	12
Both kidneys crossed....	1			Pyelogram alone.......	4

normally placed, with some edema about the right orifice Cloudy urine came from the right orifice, clear urine from the left Number 6 ureteral catheters passed apparently full distance up each ureter Through the right catheter, 15 cc of cloudy urine was aspirated The urine contained many pus cells and the same organisms as were seen in the bladder urine Ninety cubic centimeters of sterile water were instilled up the right catheter without producing pain but the mass in the abdomen seemed to increase in size and became more tender The mass decreased and became less tender as the water was withdrawn There was no residual urine in the left kidney pelvis and the urine showed no pus or organisms

Phenolsulphonphthalein injected intravenously appeared from both catheters in 4 minutes In the following 10 minutes the right kidney secreted 2 per cent, the left kidney 14 per cent, and there was none in the bladder Plain x-ray, with the catheters in place, showed the left catheter assuming a normal course while the right catheter crossed to the opposite side of the bony pelvis and lay along the left sacro-iliac joint (fig 1, 4) Pyelograms, using 125 cc of 12 per cent sodium iodide solution in the right pelvis and 12 cc in the left, showed a normal left kidney, pelvis and ureter, while the right kidney appeared as a large hydronephrosis occupying the left side of the bony pelvis (fig 1, *B*).

Because the left kidney appeared to be normal and was widely separated from the anomalous right kidney, a diagnosis of an infected hydronephrosis in a right, crossed, unfused renal ectopia was made It was believed that the right kidney, lying as it did on the lumbosacral plexus, could cause pain such as the patient was having by pressure and could also be responsible for the episodes of gaseous distention She was advised to have the ectopic kidney removed but refused operation

On October 25, 1938, she returned, with much pain in the buttocks, thighs and rectum She looked somewhat better physically than she had before and had gained some weight The mass was still present and the physical examination was unchanged The blood showed 75 per cent hemoglobin, 4,300,000 erythrocytes and 7,500 leucocytes The urine was loaded with pus Blood urea nitrogen and creatinin were normal Nephrectomy was again advised and she entered Sacred Heart Hospital

On October 29, 1938, under spinal anesthesia, a catheter was first passed to the left kidney A left lateral rectus incision was made from symphysis to above the umbilicus The anterior peritoneum was opened accidentally and through this opening the abdomen was palpated but nothing other than the retroperitoneal mass was felt A plane of cleavage was struck between the posterior peritoneum and the mass The opening in the anterior peritoneum was sutured The peritoneum was then pushed medially off the mass and the left ureter with its contained catheter identified running over the anterior surface of the mass The kidney lay to the left of the midline with its cortex directed upward and medially. There was no fat about the kidney Three good sized vessels, one from the left common iliac artery, and the other two from the bifurcation of the aorta, were doubly tied with No 2 chromic catgut The ureter entered the kidney pelvis medially across the midline, and was clamped, tied and cut A large cigarette drain was left in the depths of the dry kidney bed and the wound closed with No. 2 chromic catgut and dermol.

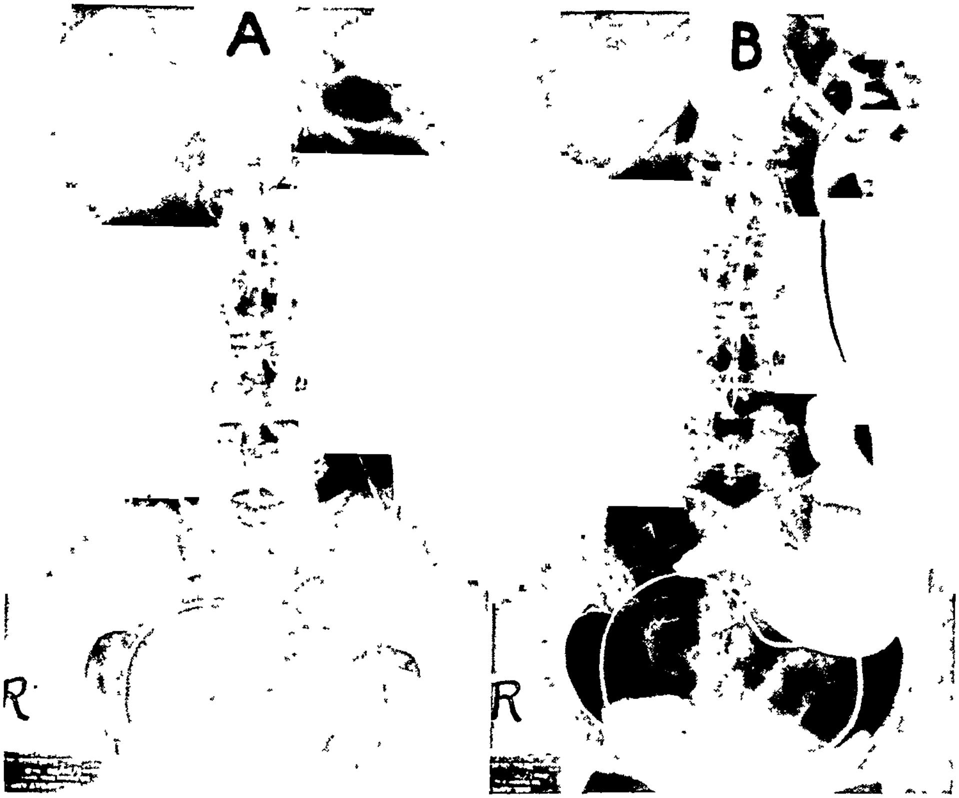


Fig. 1. *A*, Plain x-ray with catheters in place. *B*, Bilateral pyelogram. Normal left kidney. Ectopic hydronephrotic right kidney.

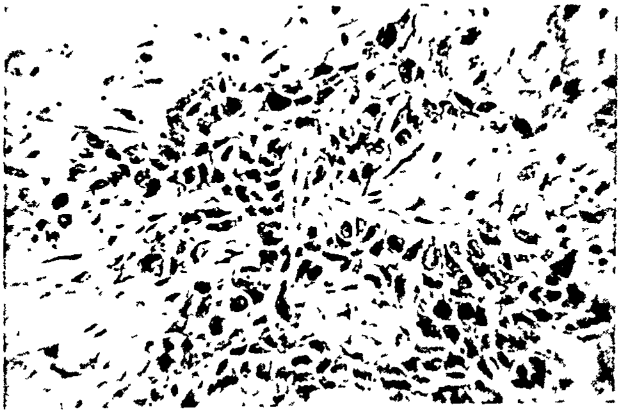


Fig. 2. Tissue from ectopic kidney

Recovery was relatively uncomplicated. The drain was gradually shortened and removed entirely on the fifth day. On the third postoperative day the pain in the buttocks and thighs was gone. She was allowed out of bed on the fifteenth postoperative day and discharged from the hospital on the twentieth postoperative day.

Pathological report (Dr. M. M. Patton): "A kidney measuring 13 by 11 by 6 cm Surface is smooth and hemorrhagic The pelvis is greatly dilated, measuring 8 cm in length and 6 cm in width The cut section shows a large caseating mass which involves the entire kidney parenchyma There is no normal secreting kidney tissue present The mucosa of the pelvis is intensely reddened The walls of the pelvis are markedly thickened and edematous Microscopic examination shows areas of atypical epithelial cells, squamous in type, which are wholly undifferentiated There is marked necrosis throughout the tissue No recognizable kidney tissue is present The atypical cells are irregular in size and shape and markedly hyperchromatic and show a marked tendency to mitosis No giant cells or tubercles are found Microscopic section of the pelvis shows marked *inflammatory changes in the mucosa and submucosa Pathological* diagnosis Degenerated squamous cell carcinoma of the kidney, primary in the pelvis, hydronephrosis, pyelitis "

Because of the finding of tumor in the kidney, x-ray films of the lungs were made but these showed no evidence of metastases or of tuberculosis

Approximately 1 year later her physician reported her death The pain in the buttocks and thighs had *recurred shortly after she returned home and she* probably died of abdominal metastases as there were large masses palpable throughout the abdomen No autopsy was done

CONCLUSIONS

Crossed unfused renal ectopia is a rare anomaly

Including the case reported herewith, 29 cases have been found Two of these cases contained adenocarcinoma

The case reported also contained a tumor but the tumor was a squamous cell carcinoma, apparently primary in the kidney pelvis and involving the entire kidney

407 W Riverside Ave , Spokane 8, Wash

REFERENCES

Alcock, N G A case of calculus pyonephrosis in a crossed ectopic non fused kidney Tr Am A Genito Urin Surg 19 299–310, 1926

Beer E , and Ferber W F L Crossed renal ectopia J Urol , **38** 541–561, 1937

Borchardt, M Med Klinik, **28** 439–441, 1932 (Quoted by Patch)

Culp, O S Renal ectopia Report of six cases J Urol , **52:** 420–429, Nov 1944

Herbst, R H Case of crossed dystopia of right kidney S Clin North Amer , 7 579–581, 1927

Harris, A Renal ectopia Special reference to crossed ectopia without fusion J Urol , **42.** 1051–1068, 1939

Harris, A Crossed renal ectopia without fusion, report of a fourth case, transperitoneal pyelotomy J Urol **48:** 252–255, 1942

Langworthy, H T and Drexler, L S Carcinoma in crossed renal ectopia J Urol , **47.** 776–783 1942

Mayers, M M Crossed renal ectopia J Urol , **36:** 111–122, 1936

Meyer, O Beitrage z path anat u z alleg Path , **44**· 1–16 1908 (Quoted by Alcock)

Nation, E F *Renal ectopia, a study of 23 cases Am J Surg* **68**· *67–72, 1945*

Patch, F S Carcinoma in a crossed heterolateral ectopic kidney without fusion Brit J Urol , **9**· 339–359, 1937

Plummer, S C Case of misplaced kidney Surg Gynec and Obst , **10:** 431–437, 1910

Resnick, B and Clark, J H Renal ectopia Demonstration of crossed unfused ectopia by fluoroscopy J Urol , **56**· 173–178, 1946

Scarcello, N S Renal ectopia A report of 2 cases with a new method of x raying pelvic ectopia J Urol , **50**· 25–28, 1943

Zide, H A and Maher, E J Crossed renal ectopia Report of two additional cases J *Urol ,* **50**· *560–567, 1943*

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

AN UNUSUAL RENAL ANOMALY: COMBINED TANDEM AND HORSESHOE KIDNEY[1]

PHILLIP B. POTAMPA, MILTON D. HYMAN AND CHARLES E. CATLOW
From the Urological Service, U. S. Veterans' Hospital, Portland, Oregon

The case that we are reporting presents such an unusual anomaly that we believe it should be included in the already voluminous literature on renal anomalies. The case shows a left tandem kidney with the superior component being drained by the left ureter; the inferior component having a common pelvis, across the midline, with the right kidney. This common pelvis is drained by the right ureter, which originates from the inferior component of the left kidney (figs. 1 and 2).

In reviewing the literature we have been unable to find any similar anomaly. Hanley reported a case of horseshoe kidney with a supernumerary kidney on the left. However, ours has no supernumerary kidney, as was proven by retrograde studies and operative exploration.

Swick reported a case of quadruple kidney in which the inferior portions were fused into a horseshoe component. Swick's patient was a 2-year-old child who showed a distinct bilateral separation of the pelves and ureters with parenchymatous fusion of both lower components. Our patient has a common pelvis for the right kidney and inferior component of the left, with the right ureter crossing the midline to drain the common pelvis from the left side.

In Wesson's book, a retrograde pyelogram is shown of a patient with a double horseshoe kidney in which the double pelves on each side are joined, while in our case, we believe there is no connection between the pelvis of the superior component on the left and the common pelvis (fig. 1, *B* and *C*).

Jacobs' patient is somewhat similar and shows a fusion of the right kidney with the inferior component of the left. However, in Jacobs' patient, the fusion forms a "cake kidney" in the midline, while ours has a common pelvis as the only apparent connection between the right and left renal masses.

ETIOLOGY

To explain the anomaly embryologically one can only point out what could have occurred. Hamilton, et al. state that the renal blastema fuse before the ureteral buds have joined with the renal masses. Lewis and Papez state that in the 10–12 mm. pig embryo the renal anlagen lie close together near the umbilical arteries. Therefore, one can theorize that as the ureteral buds grew up to meet the renal masses they may have fused across the midline. The left ureteral bud later broke away to form the ureter and pelvis of the superior component of the left fused kidney. This would account for the right ureter being implanted into the left side of the common pelvis.

---

[1] Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans' Administration, who assumes no responsibility for opinions expressed or conclusions drawn by the author.

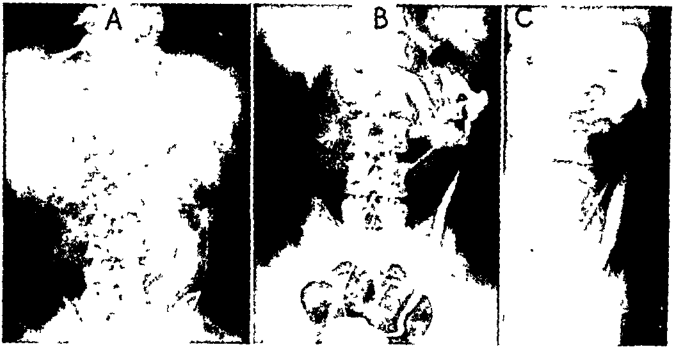


FIG 1 *A*, plain film showing catheter in right ureter passing to left of midline *B*, retrograde pyelogram showing common pelvis and pelvis of superior component of left kidney *C*, lateral retrograde pyelogram showing superior component of left kidney in paravertebral space

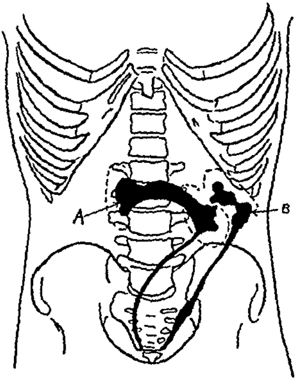


FIG 2 Diagrammatic sketch of anomaly. *A*, common pelvis; *B*, pelvis, superior component, left

CASE REPORT

A white man aged 55 was admitted to the Veterans' Hospital, Portland, Oregon, on April 7, 1947, with the chief complaints of pain and swelling in the left flank, "stones in the kidney," and "horseshoe kidney." From 1932 to 1941 he had occasional attacks of burning on urination, pain in the right lower quadrant, and "pus in the urine." In June 1941, the patient was admitted to this hospital with nausea, vomiting, and pain in the right lower quadrant. Following cystoscopy he was told that he had a "horseshoe" kidney, with a calculus in the left pelvis. He refused treatment at that time but returned again in June 1942, when he was treated conservatively for pyelonephritis. The patient was again admitted to this hospital in March 1944, at which time he had an exploration of the left kidney with removal of a staghorn calculus in the left superior renal pelvis. The operative report states that an elongated left kidney was found which was divided into two kidneys, connected by a fibrous band. The inferior portion of this kidney was continuous across the midline to the right kidney. It was also noted that the vessels lay posterior to the pelvis instead of anterior. The pelvis of the superior portion had its own ureter, while the inferior portion and pelvis from the right kidney were drained by a ureter that swung over from the right side. The patient withstood the operation well and was asymptomatic until February 1945, when he was again admitted for pyelonephritis and received penicillin therapy which relieved the signs and symptoms of pyelonephritis. Since June 1946, he had noticed a gradually increasing swelling over the operative area and has had occasional attacks of mild, colicky pain radiating from the left flank to the left groin. He had had no hematuria or passage of calculi since the last admission.

Physical examination was negative except that there was an incisional hernia in the region of the operative scar; the examination of the genitalia revealed moderate atrophy of the left testicle; and there was an area of hypesthesia over the anterior surface of the right thigh.

Laboratory data: Red blood cells 4,700,000; hemoglobin 90 per cent; white blood cells 5,300; normal differential. Urinalysis: Acid reaction; albumin negative; sugar negative; microscopic examination, loaded with pus cells. Blood urea nitrogen 29.4. Wassermann and Kahn tests negative.

Retrograde pyelography (April 1947): The plain film showed that the catheter in the right ureter crossed the midline and ended in the region of the left kidney. The catheter in the right ureter passed over to the left, to within a few centimeters of the tip of the left catheter. After the administration of dye, it was seen that there was a broad sweeping pelvis which crossed the midline from the right to left and terminated on each side in discrete pelves with their own calyces; in other words, there were in reality two pelves joined together by a connecting bridge across the midline, the bridge being convex superiorly. The fused pelvis was anterior to the vertebral column, typical of horseshoe kidney, whereas the superior component of the left renal mass was deep in the paravertebral space, the normal location for the kidney (fig. 1, *C*). Only one ureter, however, could be demonstrated to be connected with these fused pelves and this ureter emerged from the right side of the bladder and entered the pelvis to the left of the midline. In addition to this, there was also a separate pelvis on the left side which was moderately hydronephrotic. The outline of this kidney was faintly seen at its upper pole but the lower pole was superimposed upon the left part of the paired kidneys described above. The kidney outlines are sketched diagrammatically in figure 2.

DISCUSSION

One of the many interesting features of this case is the question of the possible connection between the pelvis of the superior component and the common pelvis.

As was pointed out in the protocol, when the left side was filled with dye there was no apparent dye in the horseshoe pelvis. However, when the common pelvis was filled with dye, a calyx, apparently of the left superior pelvis, was seen to fill, which had not filled when the superior pelvis was distended with dye. It may be that this calyx filled after the first x-ray film was taken so that it could be seen in the next film. Unfortunately, the patient refused another cystoscopy when we intended to clarify this point by filling the common pelvis first.

SUMMARY

An unusual renal anomaly, not previously described, is presented in which there is a tandem kidney on the left, the inferior portion of which is joined across the midline forming a horseshoe kidney with a pelvis on the right. This horseshoe kidney has one ureter which emerges from the left portion of the common pelvis. The pelvis of the superior component of the left tandem kidney has its own ureter.

REFERENCES

Hamilton, W. J., et al.: Human Embryology. Baltimore: Williams & Wilkins Co., 1945, p. 223.

Hanley, H. G.: Triple kidney with a horseshoe component. Brit. J. Urol., **30**: 165–168, 1942.

Jacobs, A.: Rare variety of horseshoe kidney. Brit. J. Urol., **15**: 55–59, 1943.

Lewis, F. T. and Papez, J. W.: Variations in early development of kidney in pig embryos, with special reference to production of anomalies. Anat. Rec., **9**: 105, 1915.

Swick, M.: A quadruple kidney with a horseshoe component. J. Mt. Sinai Hosp., **4**: 7–11, 1937.

Wesson, M. B.: Urologic Roentgenology. Philadelphia: Lea and Febiger, 1946, p. 61.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DIVERTICULUM OF THE URETER[1]

MORTON M. MAYERS
From the Department of Urology, Ross-Loos Medical Group, Los Angeles, Calif.

Diverticulum of the ureter is a urological entity which is of interest because of its rarity and because of the problems engendered by it. The term diverticulum has been liberally defined by numerous authors and as a result there are many more diverticula reported in the literature than may be unqualifiedly accepted. Although ureterocele, segmental hydroureter, hydronephrosis and vesical diverticulum have been reported as ureteral diverticula, the greatest confusion has been in the consideration of a blind-ending bifid ureter as a diverticulum.

Having reviewed the available literature on the subject, it became immediately apparent to the reviewer that a more orderly classification was a prerequisite to any proper discussion. Acknowledgement must be made to Ormond S. Culp who not only carefully reviewed the literature, but sent inquiries to the authors of questionable cases. Because of the death of some and lack of reply from others, the series must of necessity still remain incomplete and contain errors. However, it appears that Culp's analysis of the available data should be considered a base upon which other cases may be added. Stedman's *Medical Dictionary* defines a diverticulum as a pouch or sac opening out from a tubular organ, an off-shooting cul-de-sac. Obviously the blind-ending branch of a bifid ureter falls within this definition; a dilated segment of a ureter would not.

Culp points out that it is no more logical to call a blind-ending branch of a bifid ureter a diverticulum of the ureter than it would be to call a blind-ending ureter originating from the bladder a vesical diverticulum. As a working rule, Culp elected to allocate to the classification of a blind-ending branch of a bifid ureter those blind-ending hollow structures whose lumen join that of the ureter at a distinct angle, whose walls have the same coats as the ureter, and whose length is more than twice its greatest diameter. He does not deny (nor can anyone, for that matter) that a congenital diverticulum has the same etiological origin, that is, both are the result of multiple budding of the ureteral anlage.

Diverticula are divided into two main categories: 1) the true diverticulum, which is formed by a protrusion of the entire wall; and 2) a false diverticulum, which is due to the protrusion of the mucous membrane through the muscular coats. The true diverticula are apparently congenital while the false are acquired. A careful review of the cases heretofore published leads one to agree with Culp and therefore accept his classification. He presents in summary 10 cases of congenital ureteral diverticulum. Culp's case increases the number of the congenital type to 11. He reports 5 cases of acquired ureteral diverticulum to which must be added 1 case presented by Pratt, Gahagan and Fischman. The latter authors also present a case of probable diverticulum. This report is entirely based upon the report of the roentgenologist, the original films having been lost, no surgery or postmortem examination having revealed the true state It appears that for the sake of accuracy this probable case should not be accepted The present author desires to add a twelfth case to the list of congenital ureteral diverticula, thus bringing the total of reported ureteral diverticula, which may be accepted, to 18 See table 1

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, British Columbia, April 19, 1948.

TABLE 1 *Congenital ureteral diverticulum**

NO	YEAR	AUTHOR	AGE	SEX	LOCATION	SIZE	DIAGNOSIS	TREATMENT
1	1926	Stevens	59	F	L below U P junction	2 mm	Operation	Nephrectomy
2	1926	Hunner	?	F	L near bladder	?	Pyelography	Ureteral dil
3	1927	Gottlieb	50	F	L sacral	8 cm	Pyelography	Removal of stone
4	1927	Rathbun	10	M	R & L near bladder	4 × 2 cm	Pyelography	Diverticulectomy and ureteral transplant
5	1930	Chwalla	40	F	R below U P junction	cherry	Operation	Nephrectomy
6	1930	Grantham	19	M	L sacro iliac	?	Pyelography	None
7	1930	Gilmer	29	M	L U P junction	6 cm	Pyelography	None
8	1935	Brown	2	M	R sacro iliac	orange	Pyelography	Diverticulectomy
9	1942	Richardson	39	F	L mid ureter	18 cm (3500 cc)	Operation	Diverticulectomy and end to-end anastamosis
10	1944	Dodson	40	F	L near bladder	5″	Operation	Nephro ureterectomy
11	1947	Culp	20	M	L 6 cm below U P junction	1000 cc	Operation	Nephrectomy
12	1947	Mayers	39	F	L 4 cm above bladder	1 5 cm	Pyelography	Diverticulectomy and ureteral transplant

Acquired ureteral diverticulum

NO	YEAR	AUTHOR	AGE	SEX	LOCATION	SIZE	DIAGNOSIS	TREATMENT
1	1918	Bugbee	34	F	R pelvic brim	?	Pyelography	Indwelling ureteral catheter
2	1930	Chwalla	61	M	R 4 cm above bladder	3 × 1 5 cm	Autopsy	
3	1930	Crowell	?	?	L lower ureter	large	Pyelography	Diverticulectomy and closure of ureter
4	1934	Davis	35	M	R upper ureter	10 × 13 cm (500 cc)	Pyelography	Nephro ureterectomy
5	1938	Takahashi and Tsuchiya	46	M	L near bladder	egg	I V Pyelography	None
6	1947	Pratt Gahagan and Fischman	34	M	R near bladder	? 3 × 1 cm	Pyelography	Diverticulectomy with removal of calculus

* This table modified from that of O S Culp

Acquired diverticula may result from a blow out expansion of the ureteral wall above some obstruction such as a stricture or a stone or, as in Pratt, Gahagan and Fischman's case, through the site of a ureterolithotomy scar They may also form from a localized extravasation of the urine at the site of a previous ureterolithotomy or the result of accidental trauma

There is nothing specific about the symptoms, the diverticula being either the seat of a calculus or the cause of obstruction with consequent renal damage and urinary infection, with the sequelae that follow such as would be expected from any obstruction of more common origin Diagnosis was made either by autopsy, operation or by pyelographic study Treatment varied from none to cystoscopic ureteral dilatation or surgery. Surgery consisted of either diverticulectomy or nephrectomy.

CASE REPORT

Mrs. E. G. B., aged 39, was first seen in the office September 7, 1938. For 18 months previously, she had been under the care of a urologist for pain on the left side. A small calculus was discovered in the upper left ureter. Following ureteral dilatations administered over a period of 1 year, the calculus was finally passed. Ten days previous to her visit she had a temperature of 104 F. and a tentative diagnosis of pyelitis had been made. In her past history, it was noted that three Cesarean sections had been performed. She had suffered from mild dysuria from time to time. Cystoscopy was done November 7, 1938. The bladder appeared normal. There was prompt excretion with good concentration of indigo carmine from each kidney. The right pyelo-ureterogram was normal. The left ureter was dilated with moderate left pelviectasia (Fig. 1, *A*). In the upright position, there was a step-effect of the upper left ureter. At the end of 7 minutes, in the upright position with the catheters withdrawn, the right pelvis was completely emptied while the left renal pelvis was fully outlined. A

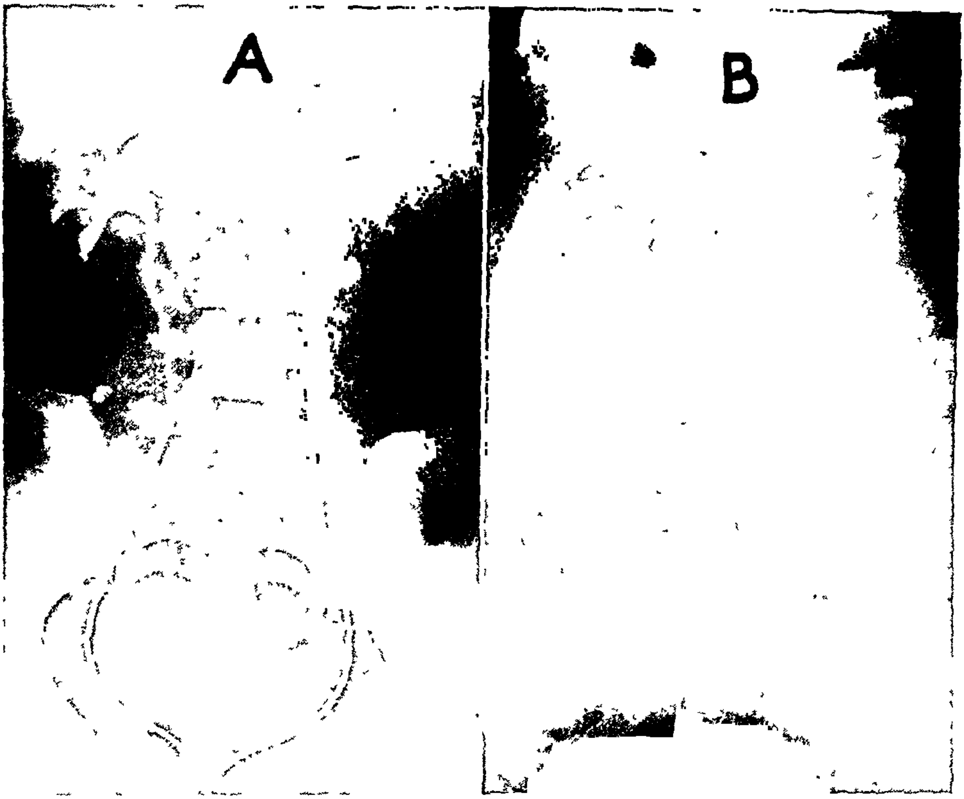
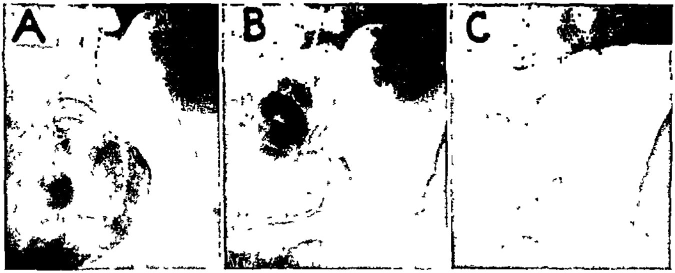


FIG. 1. *A*, left, 1938. Original pyelograms, horizontal position. Slight left pelviectasis. Lower ureter not visualized but no evidence of calculus. *B*, right, 1939. Upright position, revealing tortuosity of ureter with left ureterectasia. Spherical dilatation well demonstrated near lower portion of left ureter representing a ureteral diverticulum.

diagnosis was made of stricture of the left ureter near its vesical insertion. There was evidence of B. coli infection of the left kidney. A spherical dilatation of the lower portion of the left ureter suggested ureterocele although such was not evident in the bladder. The patient was placed on mandelic acid therapy and returned periodically for passage of dilating bougies up the left ureter. The general health of the patient improved markedly. However, due to her high-strung temperament, the patient would suffer from severe spells of nervousness following each cystoscopic manipulation, and it was necessary to prolong the time intervals between such.

March 17, 1939, pyelography was repeated (fig. 2, *A*) and it was at this time that diverticulum of the ureter was established as a definite diagnosis. On a routine of ureteral dilatations every 3 months, it was found that the patient could be kept in satisfactory state of health, despite a low-grade infection of the kidney.



[illegible] *ureteral diverticulum partially filled, 4 cm. of ureter* [illegible] No evidence of calculus *B*, middle, large calculus [illegible] left ureter. *C*, right, calculus seen surrounded by

By the end of another year, episodes of pain on the left side, with exacerbations of urinary infection, were increasing. Surgery was urged but the husband requested that the patient be not informed of the real nature of her condition, as she would refuse surgery under any circumstance. As a result the usual cystoscopic manipulations were continued and the patient was again restored to seemingly good health; but on December 7, 1941, a temperature of 103 F. supervened, accompanied by severe pain on the left side. There was some remission under sulfathiazole therapy. Cystoscopy was subsequently performed at which time a plain film revealed the presence of a marble-sized calculus in the diverticulum which previously had contained no calculus (fig. 2, *B*). Further studies had revealed an abrupt spherical dilatation, 1.5 cm. in diameter, located about 5 cm. above the left ureteral orifice with normal calibration of the ureter below that point and only moderate dilatation of the ureter above the site of the presumed diverticulum (fig. 2, *A*).

Surgical intervention was insisted upon. Again the patient wished to procrastinate but because of recurrence of fever and pain, prompt hospital admission was necessitated. Physical examination was essentially negative except for tenderness over the left costovertebral area. The temperature was 103 F., the blood pressure 128/94. The urine contained pus cells. The hemoglobin was 77 per cent; leucocytes 11,600. At cystoscopy 25 cc cloudy urine was aspirated from the left pelvis after overcoming a point of obstruction at 6 cm. Indigo carmine was markedly delayed in appearance from the left side. An 8 F. ureteral catheter was tied in place for continuous drainage. Gram positive cocci and gram negative bacilli were noted on the stained smears from the left kidney urine. Five days later the temperature had become normal; the patient's general condition and mental attitude had markedly improved, a factor which had always been a great problem in management of her case.

On December 22, 1941, an operation was performed, consisting of a suprapubic cystotomy with transvesical extraperitoneal exposure of the lower portion of the ureter, ureterolithotomy and ureteral diverticulectomy. The bladder was opened in the usual manner. The intramural portion of the left ureter was incised. The incision was then prolonged upward through the entire thickness of the bladder wall in an oblique direction, following the course of the ureter but not cutting into the ureter, the indwelling ureteral catheter being used as a guide. The ureter was freed and the catheter was removed. It was then attempted to free a sufficient length of the ureter so that it could be resected above the diverticulum and re-implanted in the bladder in such a manner so as to preserve the valve-like action of the bladder wall (employing the technique which Elmer Hess used successfully in the treatment of impassable stricture of the intramural portion of the ureter). After freeing the ureter to a point above the diverticulum, it was determined that resection of the necessary 7 cm. of ureter would leave the ureter too short to permit anything but a high re-implantation and this it was desired to avoid. About 5 cm. above the vesical end of the ureter there was a bulbous thickening of the ureter eccentrically placed in relation to the long diameter. The wall of this bulbous portion was considerably thickened. The incision made through the wall of the diverticulum revealed this thickness to be muscular hypertrophy. The calculus was removed, portions of the wall of the diverticulum were resected, and the opening into the ureter was closed. The bladder wall was closed over the exposed ureter with interrupted sutures, loosely tied. The original bladder incision was closed tightly in the usual manner. A Foley catheter was inserted through the urethra for drainage.

The postoperative convalescence was fairly smooth, both catheters being removed on the eleventh day. Because of considerable suprapubic leakage, the urethral catheter was replaced. Cystoscopy was performed January 5, 1942 and despite edema of the trigone, a catheter could be passed up the left ureter with ease. She was discharged on the fourteenth postoperative day; 3 days later the catheter was removed and voiding was normal.

Cystoscopy and ureteral catheterization were performed at intervals to March 6, 1942. By the latter date there was no evidence of cystitis. The trigonal elevation had almost disappeared. The ureteral orifice on the left was easily catheterized with an 8 F. catheter. Pyelography revealed some dilatation of the left renal pelvis, inferior calyces and upper pelvis, as previously. The lower left ureter terminated cleanly at the bladder as demonstrated by the ureterogram (fig. 3 *A*). There was no evidence of the recent diverticulum. Cultures of the urine from the left kidney were still positive for B. coli. The patient returned in 1945 for cystoscopy but no pyelograms were made. On January 9, 1948, a final cystoscopic check-up was made. The patient had been entirely free of symptoms. Her nervousness was a thing of the past. She had had no real illness for 4 or 5 years. The bladder was entirely normal, except for a somewhat aberrant location of the left ureteral orifice. The urine was clear, grossly

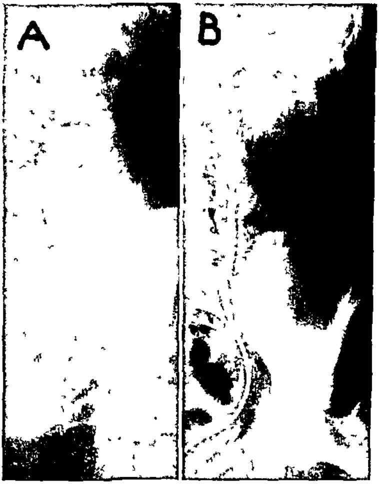


FIG 3 *A*, left, 1942. Postoperative result Lower left ureter shows no evident dilatation Both calculus and diverticulum are no longer evident Cystogram (not shown here) revealed no evidence of reflux *B*, right, 1948 (six years postoperative) Upright position. Apparently normal contours of pelvis and ureter

and microscopically. Pyelography revealed the left kidney to be essentially normal except for a minimal amount of pelviectasia (fig. 3, *B*). In the upright position, there was only moderate descent of the left kidney, as compared with the preoperative pyelogram (fig. 3, *B*).

DISCUSSION

Because of the rarity of ureteral diverticulum, it was not difficult to overlook the presence of such a diverticulum which could be revealed only if the lower ureter were well delineated with radio-opaque material. Consequently, for a period of several years, the patient was treated for an apparent stricture without recognition of the true condition. Even after the true condition was recognized and surgery appeared to be indicated to relieve the cause of obstruction, the patient's disposition was such that conservative therapy was carried out and the patient was thereby maintained in a satisfactory state of health. At some unknown time subsequent to the onset of treatment a calculus developed in the diverticulum. It was only after conservative treatment no longer resulted in relief to the patient, that she reluctantly consented to surgery.

947 W. 8th St., Los Angeles 14, Calif.

REFERENCES

Culp, O. S.: J. Urol., **58**: 309, 1947.
Dodson, A. I.: J. Urol., **52**: 526, 1944.
Pratt, J. G., Gahagan, H. Q. and Fischman, J. L.: J. Urol., **58**: 322, 1947.
Richardson, E. H.: J. Urol., **47**: 535, 1942.

THE JOURNAL OF UROLOGY
Vol 61, No 2 February 1949
Printed in U S A

THE LOOPED CATHETER URETERAL STONE EXTRACTOR: PERPLEXITIES IN ITS CONSTRUCTION AND USE[1]

MILO ELLIK

The existence of some confusion concerning problems met in the construction and performance of the looped catheter stone extractor prompts this report

Experiences of myself and others have proved this instrument a most efficient one if properly constructed, protected and tested before being used However, certain rules must be followed if top performance is to be achieved The slightest deviation may lead to confusion, distrust and finally to dissatisfaction on the part of the operator

SUGGESTED RULES FOR CONSTRUCTION

I have not yet seen a completely satisfactory commercial model of the instrument Plans for my modified version have been released to one of our excellent catheter manufacturers and if it can be properly constructed, will become a desirable ready-made model Until this is available I shall continue to, and may always, make my own The home-made device can be constructed by anyone willing to use the time and care necessary Very good ones are made by nurses who find such delicate work simple and easy Comparative figures show that the cost of home made models is about half that of commercially available ones

A new No 5 whistle tip ureteral catheter is the routine choice The only necessary modification of this catheter is the creation of a hole, slanting toward the caudad end, on or very near the 6 cm marker This hole may be made with a No 24 hypodermic needle held in a hemostat (fig 1, *A*) After heating the needle red hot on a Bunsen burner the new opening can be made by repeated gentle punctures without mutilating the catheter This hole should be made on the same side as the lowest lateral eye so that this eye on the inner curve of the closed loop protects the catheter from cracking in that area Any debris that the needle may push into the lumen should be removed by the passage of a stiff catheter stylet

The other phase of construction consists of threading the filament I use steel surgical suture wire in 7 foot lengths The size of this wire may vary but usually some gauge between No 32 and No 35 is used The smaller this gauge the less tendency there is for kinking, but a larger gauge contributes a desirable amount of additional stiffness to the catheter A new filament should be threaded through the catheter after each use of the instrument or until the life of the catheter has terminated With vigorous handling this life might be that of a single stone It is mandatory that filaments do not become fouled and that no kinks exist within the lumen of the catheter These spoil performance and might even prove dangerous

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, B C, April 21, 1948

It has been my custom to thread the first portion of the filament downward through the distal eye until it appears at the base, to be fastened there as the anchor. The other end of the filament is threaded downward through the newly created hole until it too appears at the base. It is then withdrawn completely to act as the pull filament (fig. 1, *B*). This pull filament will be a foot or more in length and needs no handle. A sharp kink of the wire as it exits from the distal eye helps anchor the filament and streamlines the instrument for insertion into the ureteral orifice. No movement of the anchor half of this double filament is anticipated or desired during manipulation. The portion of the wire which appears outside and parallel to the distal 6 cm. of the tip of the catheter should always be a portion of the pull filament. The reverse of this creates a potentially dangerous situation. The anchor filament may be fastened to the caudad end of the catheter in numerous ways (fig. 2, *A*). My personal preference is the bead method. Convenient beads consist of tiny, sliced-off ends of catheter bases, perhaps even of the one being used. The anchor wire can be tied to this bead. Any type of glass or metal bead of similar size would serve the same purpose. The wrap-around method of anchoring the wire, as described by Balkus, has one fault in that it frequently becomes fouled when the cystoscope is removed. Instead of handles the wire may be wrapped around one's gauze-protected forefinger (fig. 2, *B*).

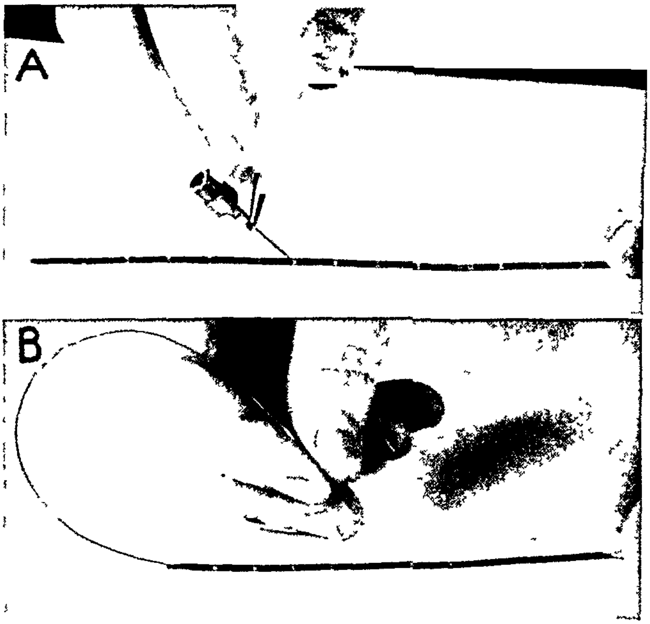


FIG. 1. *A*, above, repeated gentle punctures with a red hot hypodermic needle at the 6 cm. marker forms an adequate eye. *B*, below, Pull filament is threaded downward through new eye after anchor filament has been placed.

I prefer wire to any other filament in spite of its tendency to kink. Although more pliable materials may sometime prove superior, they do not contribute to desirable extra stiffness in the instrument's tip. This extra stiffness can be *most helpful when insinuating the instrument by a stone and in keeping the* looped portion well spread open against muscular contractions of the ureter. When, and if, catheter manufacturers build in this extra stiffness, perhaps more pliable materials than wire will become the choice of filament. It is conceivable that such materials might obviate the necessity for constant restringing. Wire has shown less tendency to become twisted and fouled within the lumen of the catheter, thus virtually eliminating this hazard. So far it has seemed advisable to use a double filament because this permits its removal in situ and might therefore be considered a safety factor. However, my experience has never found this theoretical safety factor necessary.

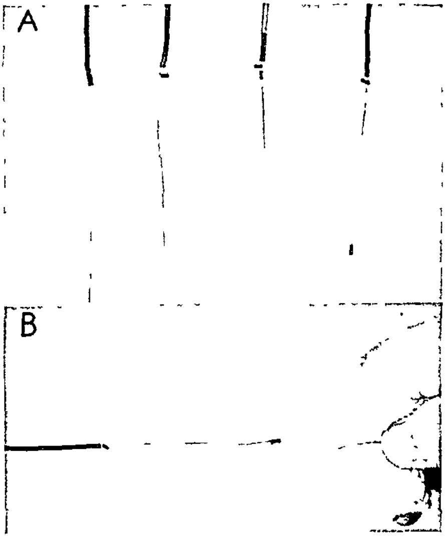


Fig. 2. *A*, above, Balkus wrap-around and bead methods of anchoring. Second bead on pull filament indicates whether loop is open or closed. *B*, below, common method for traction. Separation of two beads indicates closure of loop

Wire filaments should be carefully prepared and preserved before insertion, to avoid kinking. Seven foot lengths of wire suspended and held taut by means of a suitable weight prove most satisfactory. Kinks occurring at either end may be sheared off at right angles with a scissors. Right angle shearing produces a blunt end which will aid in threading the filament. Lubrication of the lumen is optional before threading but may be considered an aid to performance.

SUGGESTED RULES FOR STORAGE AND STERILIZATION

The completed instrument should be stored without bends or kinking. A tube type catheter container or cloth roll serves well. At the time of sterilization care should be taken to avoid all but the most necessary bending—the longer the sterilizer the better. Keeping the instrument straight prevents undesirable kinks in the wire. If sterilization is done by boiling, follow-up emersion in a cold solution will insure the return of maximum rigidity.

SUGGESTED RULES FOR INSERTION AND MANIPULATION

Each extractor should undergo close scrutiny by the operator just prior to insertion. The looped portion should always be inspected. The instrument should be grasped between thumb and forefinger at the level of the newly created hole while the other hand manipulates the pull filament (fig. 3). The loop need not be completely closed at this test, partial closure suffices and avoids unnecessary kinking. If the looped portion responds well outside the ureter, it can be depended upon to perform similarly within.

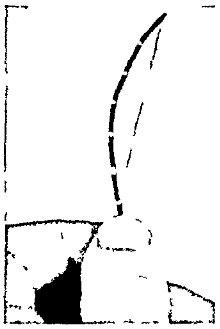


Fig. 3. Level at which instrument should be held in testing for smooth performance prior to insertion.

Insertion of the extractor should not be preceded by insertion of other ureteral catheters as these might shift the axis of the stone, making it impassable. If, however, the extractor cannot be passed, other catheters may then be used to advantage. Insinuation of the latter in 4 or 5 F. sizes is sometimes possible in such instances. One of these left alongside the calculus for a few minutes and then gently withdrawn may facilitate insertion of the extractor. Because of possible kinking, fouling, or distortion of wire filaments, the extractor should not be twisted at any time during passage.

When ready to close the loop, the operator may choose to relinquish the cystoscope to an assistant who holds it pointing directly at the ureteral orifice and as nearly in line with the course of the ureter as possible. The loop is formed by pulling on the pull filament and pushing on the catheter with the opposite hand. This should be done slowly to preserve tactile sense. Should the tip of the instrument be in a calyx, resistance will be felt and slight withdrawal will be necessary to permit the loop to close. Usually the extractor will pass all the way to the renal pelvis once it has passed the calculus. Formation of the loop is easier within the pelvis than in ureter. The loop can be formed within the less spacious ureter, however, providing the entire length of the looped portion can be insinuated past the stone. Pelvic closure is desirable, if possible. Complete and satisfactory formation of the loop is determined in several ways. One of these is by measuring the length of pull filament which appears outside the catheter after traction (fig. 2, *A*). Another method is by x-ray visualization. The operator can usually feel a slight tap as the tip of the catheter strikes its side. Markers of various types can be installed on the pull filament and may prove reassuring to the operator. Any indecision as to closure at this critical point can of course be dispelled by x-ray visualization.

SUGGESTED RULES FOR TRACTION

Withdrawal of the loop toward the stone must be done very slowly. A good rule is to withdraw at the rate of 1 cm. of catheter every 10 seconds. Withdrawal must never be jerky but rather with exaggerated deliberation. This is especially true when the loop first contacts the calculus. At this point will occur the initial hang which indicates that the tip of the loop has touched the stone; it does not necessarily mean that the calculus has become encircled (fig. 4). Prior to this first hang the loop slides down the ureter with no sensation of obstruction. All traction should be confined to the pull filament to insure constant closure of the loop. The hang of the loop against or encircling a stone is unmistakable but the x-rays alone can prove which has occurred. It should be remembered that some smaller calculi will ride on out ahead of the loop and never require actual snaring. Most stones will remain sufficiently impacted to resist the first contact with the loop's tip and as this slides by, encirclement produces the second and final hang. The quick release of the first hang as the tip of the loop slides by the stone is quite startling. The operator must watch carefully for this and cease traction at once to avoid pulling the loop entirely past the calculus before it has an opportunity to become settled within the confines of the opening. Should this maneuver not be observed engagement will be lost and insertion of another extractor necessary. Furthermore, such an occurrence might impact a previously passable stone more firmly and perhaps make it impassable. Roentgenological proof of engagement is entirely optional but it can be of academic interest, and it serves as a permanent record. The unmistakable hang produced by a well-encircled stone is practical

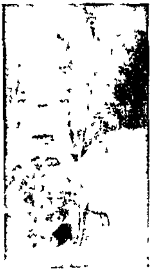


FIG. 4. Initial hang occurs when tip of loop contacts calculus. Encirclement follows further deliberate pull. Air in renal pelvis was used to facilitate passage of instrument.

proof of the desired result and usually can be depended upon even in the absence of x-ray evidence. In the absence of stone, the loop simply does not hang until its tip reaches the ureteral orifice. At this point the tip can be seen cystoscopically and this obstruction obviated by a slight twist with additional traction.

When engagement is certain, it is best to remove the cystoscope before traction is instituted. This eliminates an undesirable impediment. If the stone yields readily there can be no contraindication to pulling it out slowly and at once. However, if the impaction holds, after a pull of several minutes, it is advisable to stop all traction and reapply this force some hours later. During the interim the redundant portion of the instrument can be looped on, and taped to the patient's abdomen. It is advisable to enclose the end of the extractor in sterile gauze for absorption of urinary drainage. This tactful period of waiting is advantageous because it allows time not only for the ureteral musculature to seat the stone symmetrically within the confines of the loop but also for the accumulation of a soft lubricating mass of mucus within and around the area. Experience has proved the wisdom of this period of arbitrary waiting which frequently extends over a 12 hour period.

I have never used weights, pulleys or other similar devices for prolonged and continuous traction. Such unsupervised pull, although probably not at all dangerous, risks the unseating of the stone prematurely. I prefer the more substantial and reliable manual traction at intervals. This should be done by either the operator or one of his enlightened associates. Such traction performed two or more times daily suffices and most calculi will come away within a 24 hour period. These sessions of traction are usually not sufficiently painful to the patient to require the use of an anesthetic or even opiates.

Traction should never exceed 4 pounds of sustained pull; usually less than 2 pounds is sufficient. If actual measurement of this is desired, a small spring scale can be used (fig. 5, *A*). Another safety device may consist of a linen thread attached to the pull filament (fig. 5, *B*). Such a thread having a known breaking point or tensile strength of less than 4 pounds breaks before this dangerous limit is reached. The experienced operator will soon find that he is able to stay within the limits of safety without the aid of such implements. The period of time during which deliberate manual traction may be continued depends upon the discretion of the operator; if the stone will not yield after a steady pull of 20 minutes, however, it is usually discreet to discontinue traction until a later time.

When an engaged stone slips through the ureteral orifice, elimination of the previously described hang is sudden and unmistakable. When this occurs the ureteral orifice is within or at least against the bladder neck. This phenomenon proves favorable for two reasons: 1) The bladder neck acts as a convenient brace; and 2) the lumens of ureter and urethra become almost, if not entirely contiguous. This not only protects the ureter from fracture but allows the stone to continue its course through a somewhat larger but similarly shaped tube. Because of this fact the majority of stones deliver through the external urinary meatus still encircled by the instrument. Occasionally, however, the stone may drop into the bladder or be shattered into sand by the pressure exerted by the ureteral orifice. In either instance evacuation with or without lithotrity requires transurethral instrumentation. Litholapaxy has been necessary on a number of occasions in the author's experience with this extractor.

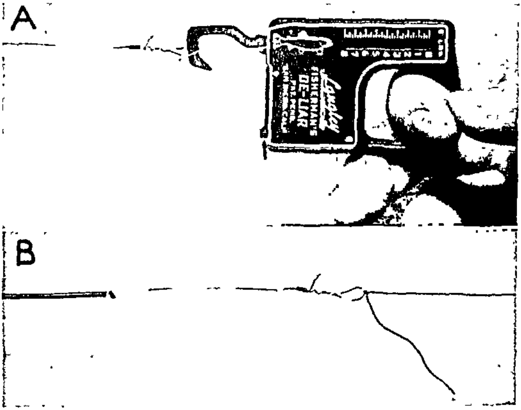


Fig. 5. *A*, above, small spring scale used as safety device to measure amount of traction. *B, below, thread, with known breaking point below 4 pounds, attached to pull filament* will avoid dangerous amounts of traction.

SUGGESTED RULES FOR FOLLOW-UP

Cystoscopic review of the ureteral orifice and catheter exploration of the ureter are optional following the extraction of stone but may be comforting to the operator. Experience has shown that indwelling ureteral catheters are not necessary or desirable after such a procedure. Chemotherapy and antibiotics are reserved for the rare febrile patient or for the cases of persistent pyuria. Early ambulation and forced fluids are encouraged for obvious reasons. The wisdom of follow-up pyelographic studies need not be reiterated, but it should be mentioned that these have never shown any evidence of permanent or undesirable ureteral damage as a direct result of such instrumentation. The very occasional ureteral meatotomy necessary has proved easy though the extractor might be in situ.

OFFICE VERSUS HOSPITAL EXTRACTIONS

Cystoscopic extractions of ureteral stones with any type of instrument could hardly be classified as desirable office procedures. With the looped catheter an office procedure can be considered in an occasional case. Very little pain occurs and patients suffer negligible discomfort as a rule. Anesthesia is considered more of an aid to the operator for relaxation of ureteral musculature. In case a stone engaged during office manipulation resists immediate extraction, the free end of the extractor may be taped to the patient's abdomen, and the patient become normally ambulatory to await hospitalization or return to his home. Should hospitalization be entirely out of the question for financial or other reasons, daily supervision in the home or office may suffice. The author knows of 1 case, not his own, in which a large ureteral stone was extracted in this manner over a period of 12 days. The patient lost no time from work; he reported to the urologist's office for daily periods of manual traction until the stone was delivered. The absence of pain and fever in this case represents the usual picture in cases in which the extractor is allowed to remain in the ureter over a period of days. Canalization about the loop permits excellent drainage and the ureter is splinted against painful contractions.

SUMMARY

This report covers a period of 34 months of personal experience with this instrument. During that period 131 stones of various types, size, and location have been extracted. My statistics remain similar to those already published. No further undesirable accidents, no need for surgical interference and no deaths have occurred. The additional year of experience seems to have emphasized at least two important points: 1) that one cannot be too meticulous in the construction and care of this device; and 2) the wisdom of allowing an engaged calculus to remain in the ureter without more than the initial short period of traction for variable periods up to 24 hours before concerted traction is instituted.

The passage of time has served only to fortify my personal approval of this mode of ureteral stone extraction when such a procedure is indicated.

117 E. 8th St., Longbeach 13, Calif.

REFERENCE

Ellik, M.: Stones in the ureter: their extraction by looped catheter. Tr. West. Sect., Am. Urol. A., **13**: 45–50, 1946; also, J. Urol., **57**: 473–478, 1947.

THE JOURNAL OF UROLOGY
Vol 61 No 2 February 1949
Printed in U S A

EARLY DIAGNOSIS AND PROPER TREATMENT OF CANCER OF THE URINARY BLADDER[1]

GILBERT J THOMAS

Statistics of the last two 5 year periods show that 3.8 per cent of all cancer deaths in this country are caused by tumors of the urinary bladder. This is due to inaccurate and misleading diagnostic data, and to our surgical therapy which has not aimed at a cure by complete removal of all the cancer and cancer bearing tissue. Microscopic examination of the entire tumor, its grade of malignancy, extent of spread and metastases present were not always known before treatment was begun.

When dealing with any cancer, the general surgical dictum is: "Early diagnosis and early complete removal." Urologists' past experience with cancer of the urinary bladder suggests that their dictum should be: "Early accurate diagnosis, followed immediately by early complete surgical removal!"

OCCURRENCE

Of all admissions to large urological services in general and teaching hospitals, 14 per cent are for hematuria, 30 per cent will have tumors of the urinary bladder, 41 per cent of the bladder tumors will be found on the floor or trigone. There will be 4 times as many males as females.

ETIOLOGY

Little is known about the exact causes of cell and tissue changes in the mucosa or bladder wall that develop into malignant tumors. Animal experiments, together with clinical research and observation, suggest that mechanical and chemical irritation play some part in the formation of these tumors. The occurrence and growth of spontaneous bladder tumors may bear some etiological relationship to continuous contact of the mucosa with unrecognized chemical or other carcinogenic agents encountered by workers in the aniline dye and other industries. Arsenic was recovered from multiple papillary tumors of the ureter and urinary bladder in a patient who ingested large quantities in the form of Fowler's solution.

Pathologists recognize a carcinogenic predisposition possessed by the cells of the epithelium and other structures of the urogenital system. Recurring papillomata of the bladder mucosa suggest continuing activation of the predisposed cells to unrecognized carcinogenic agents within the urine or the blood stream.

To determine possible carcinogenic stimulating activity, tests were made of 1,028 chemical compounds with which the average person might come in contact in his ordinary pursuits. Of these, 248 were active stimulators that induced cancer formation in experimental animals of different species.

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, B. C., April 20, 1948.

To a considerable extent, cancer in man is an environmental and occupational disease. Frequent occurrence of bladder floor tumors where continuous trauma is produced by the constant presence of urine that may contain carcinogenic substances, may be related to this trauma acting as an additional etiological factor.

Another etiological feature, when considering tumors of the bladder found on the trigone and extending into the prostatic urethra, is the possibility that these tumors, as those originating in the prostate gland, may be gonad related. Excellent results have been reported when estrogenic substances were used parenterally, together with other treatment, in male patients with cancers of the bladder extending into the prostatic urethra.

Thomas J. Kirwin is convinced that papillomatosis of the urinary bladder is due to a filterable virus. Recent reports suggest that certain tumors of the female breast are caused by a virus.

SYMPTOMS

When no other lesions in the bladder are present, the first symptom or finding reported by the patient is hematuria, usually painless; unless the tumor is located at the bladder neck or accompanied by severe cystitis, hyperplasia of the prostate gland, or a foreign body. Microscopic blood cells in the urine may be the first and only finding. The presence of blood cells in any patient's urine is a positive indication for immediate, complete urologic examination which should include clear cystopyeloureterograms. Tumors of the bladder may accompany prostate gland hyperplasia and cancer, so that when possible and not contraindicated by other constitutional disease, a cystoscopy should be done in all patients with bladder neck obstruction.

EARLY DIAGNOSIS

The American Urological Association has maintained a carcinoma registry for many years in the Army Medical Museum at Washington, under the direction of Colonel Ash. Pathologists at the Registry have examined thousands of specimens of tumors of the urinary bladder, sent by urologists and other surgeons in all parts of the United States and Canada. These were submitted to microscopic examination and a diagnosis of the presence or absence of malignancy obtained. If malignancy was present, its grade was estimated. A certain amount of clinical data and the urologist's findings when the tumor was inspected through the cystoscope accompanied each specimen.

The diagnosis of the specimen, following microscopic examination and grading, was accepted as representing the cellular structure of the entire mass. Sometimes no attempt was made to obtain the original biopsy specimen of tissue from the most suspicious area, or from the adjacent bladder wall. Biopsy specimens were removed through the cystoscope, with rongeurs or other special specimen-taking instruments, and since the advent of the resectoscope, with the activated loop of this instrument. Specimens obtained in this manner did not always represent the cellular changes that may have occurred in the entire tumor, and the pathologist was handicapped when the electric loop was used.

This might change the cellular architecture of the specimen, so that a satisfactory diagnosis could not be made of malignancy and its grade

Following bitter experience, most urologists have learned that all tumors of the urinary bladder are malignant and that "no tumor located here is better than its worst part" It is impossible during every cystoscopic examination to obtain a clear view of the entire tumor with its attachments to the bladder wall, and the character of the adjacent bladder wall mucosa When these conditions exist, a specimen from the proper area of the tumor and its attachment may not be obtainable transurethrally The cystoscopist can make the more accurate diagnosis of the presence of malignant change and its grade when it is possible to make a satisfactory examination of a bladder tumor, so that all areas including its attachment to the bladder wall can be easily inspected

Dr Archie L Dean, who has had wide experience in diagnosing and treating carcinoma in the urinary bladder, reported that in 58 per cent the microscopic examination of the entire bladder differed from those made on biopsy specimens removed through the cystoscope In 50 per cent of the patients operated on, the true condition was of a greater degree of malignancy than that found in the cystoscopic biopsy specimen

During the first seminar conducted by the Urology Branch of the Los Angeles County Medical Society, Dr J R McDonald said that pathologists have not always given proper pathologic information to surgeons and urologists He emphasized the importance of classification into cell types, as squamous, transitional and adeno Combinations of these cell types may occur in the same tumor Dr McDonald suggests the following criteria as all important in the pathological diagnosis of carcinoma of the urinary bladder

1) Type of carcinoma cell squamous, adeno or transitional

2) Is it papillary without infiltration, papillary with infiltration, or just infiltrative?

3) Has the infiltration extended? Is it confined to the wall of the bladder, or has it extended into the perivesical fat?

4) Has vascular invasion occurred?

The grading of the malignancy of these tumors fits well into this diagnostic scheme

Inaccurate pathologic diagnoses of bladder tumors have delayed radical surgery The resectoscope which permits transurethral removal of these tumors with the cutting current and at the same time the fulguration of the adjacent bladder wall, has further delayed proper radical surgery of this death-taking disease While the resectoscope may permit complete removal of the tumor, including portions but not the entire thickness of the bladder wall, it does not permit the surgeon to see through the bladder wall so that he does not know whether invasion has occurred into the perivesical tissues

In addition to endoscopic inspection of tumors in the bladder and removal of tissue for biopsy, there are other diagnostic examinations not used by many surgeons The first one is the careful bimanual palpation (under anesthesia when necessary) of the bladder and adjacent structures This examination will give much useful information that cannot be obtained through the endoscope or cystoscope.

Papanicolaou and Marshall examined the urinary sediment from 83 patients suspected of harboring cancer in the genito-urinary tract. In 27 they found positive evidence and made a diagnosis of cancer without knowing clinical findings. In 88 per cent of the cases reported positive, the diagnosis was confirmed by autopsy or clinical observation. There were no false positive reports, but there were 40 false negatives. This examination is based on the observation that there is a continuous superficial desquamation of cells from tumors, in such a proportion as to permit their identification, and therefore the diagnosis of cancer from urine sediment smears. This method of examination is simple and inexpensive, but interpretation is difficult and special training is needed to read the results. This method of examination is more useful in patients who have had bladder tumors removed, and when cystoscopic observation is impossible. It will reveal the presence of cancer cells suggesting recurrence, or the possibility that the entire tumor has not been removed.

Dr. McDonald described a simpler method of staining cells in urine sediment. He stresses the difficulty of interpretation but believes that this method of detecting cancer cells, which means cancer somewhere in the urinary tract, will increase in popularity. However, finding no cells in urine sediment does not mean that there is no cancer. Dr. McDonald was unable to determine the anatomic location of the cancer when he detected the presence of cancer cells. These were so changed that they did not resemble the cells forming the tissue from which they came.

There are many methods of examination which should aid us in making accurate diagnosis of the presence of malignancy and its grade. I consider every bladder tumor potentially malignant. Dr. Clyde Deming and his co-workers were able to transplant grade 1 papillomas of the human bladder into the anterior chamber of the eye with heterologous growth. This growth proves that papillary grade I tumors are true cancer.

The urologists' record of cure of bladder tumors, using the methods of diagnosis and treatment now in vogue, is not a good one. Local recurrences are frequent and should have been expected when using transurethral methods of treatment.

Transplantation of cancer cells in the same host may still be possible, but most pathologists and those interested in cancer research believe that certain tissues have a carcinogenic predisposition and that certain substances in the urine or blood stream may activate malignant growth in all epithelial areas of the urinary tract. We still find many reports of the transplantation of cancer cells in the ureter and in the bladder from papillary tumors that were primary in the mucosa of the renal pelvis. A statistical study of many papillary cancers of the renal pelvis reveals comparatively few transplants in the bladder and ureter.

When there is doubt as to the diagnosis and character of a tumor of the urinary bladder, surgical exploration must be done. To be complete, this should be exploration of the abdominal cavity, including search for evidence of enlarged nodes in the pelvis and adjacent to the large blood vessels, and metastatic nodules in the liver. The peritoneal surface extending over the urinary bladder must be visually inspected and palpated for evidence of invasion. The bladder should then be opened and a biopsy specimen obtained, compared with the biopsy taken transurethrally, and an inspection made from within the bladder to determine how invasive the tumor has been. Has it invaded the perivesical tissues, especially the fat in this area?

Dr. Jewett examined the pathologic changes in 107 cases of infiltrating carcinoma, to determine conditions under which local extension and metastases occurred. Group 1, 3 cases: The deepest penetration in the bladder wall was to the submucosa. Group 2, 15 cases: The growth extended into but not through the muscularis. Group 3, 89 cases: The growth had penetrated through the muscular layers. In group 1 no evidence of spread could be observed. In group 2 86 per cent were free from spread. In group 3 only 26 per cent revealed no evidence of spread. Since potential curability can be considered to exist whenever no spread has occurred, the drop in curability after the perivesical tissue had been reached is statistically significant. Metastases were less frequent when the tumor was located in the posterior wall.

TREATMENT

Proper treatment of cancer of the urinary bladder depends primarily on accurate diagnosis. If the operator is satisfied that he is dealing with grade 1 malignancy, transurethral resection and fulguration may be applied. This patient must be reexamined at the end of 3 and 6 months. On recurrence transplantation of the ureters and complete removal of the bladder, after proper inspection for evidence of metastases, should be done. When metastases are present, or if the patient is not in good physical condition, transplantation of the ureters should be done and the tumor of the bladder treated with heavy doses of X or radium irradiation. Follow-up reports from patients who had transurethral resections of bladder tumors, have shown few recurrences, and many urologists have used this experience as a basis for continuing transurethral methods of treatment of all bladder tumors.

Dr. Gershom Thompson, reporting on follow-up data obtained 5 years after transurethral removal of over 300 tumors, found: 77.2 per cent of grade 1 malignancies well, 67 per cent of grade 2, and 22.6 per cent of grade 3. This is the best report of which I know. His pathological reports on tissue removed before operation were accurate. He removed the bits of tissue with a cold knife so that the specimens were not changed as occurs when the electrically activated loop is used.

Grade 2 malignancies, immediately after surgical exploration for evidence of metastases, should be treated by segmental or complete resection of the bladder and diversion of the urinary stream. The ureters should be placed in the bowel or in the skin. Grade 3 and 4 malignancies should be treated in the same manner. When the only method that can be applied is palliative, it should be diversion of the urinary stream. By this treatment, many patients' general condition has been improved and 2 or 3 years added to their life expectancy.

If the tissues of the urogenital tract possess carcinogenic predisposition and the urine or the blood stream may contain carcinogenic activators, then it is understandable that malignant tumors may regress in size and activity after diversion of the urinary stream. Ureteral transplantation prolongs life because many patients, with inoperable carcinoma of the bladder, die of uremia resulting from obstruction of the lower end of both ureters and not from the toxemia associated with extensive cancer.

The operation of cystectomy, diversion of the urinary stream, is a formidable one, but does produce cure when the cancer is accurately diagnosed and treated early. At the Mayo Clinic in 1940, a cystectomy was done in 20 per cent of bladder tumors, while in 1946, cystectomies were done in 49 per cent.

We must encourage the younger surgeons to attack cancer boldly, and they should be taught how to divert the urinary stream without additional operative mortality. They must aim at cure, not palliation, unless that is the only possibility. We should insist that every patient with a history of hematuria, or whose urine reveals the presence of blood cells in the urinary sediment, should be thoroughly examined, not the second time, but the first time the patient notices hematuria.

In reviewing the records of 32 patients who had cancer of the urinary bladder during the last year, only 4, or 12.2 per cent, after careful surgical exploration, were fit subjects for cystectomy and diversion of the urinary stream, or any attempt at cure. Some had transurethral surgery instead of radical surgery, and many did not report to the hospital or the doctor.

CONCLUSIONS

Cancer of the urinary bladder caused 3.2 per cent of all cancer deaths. Morbidity and mortality rates have not lessened.

Micro- and microscopic blood in the urine means cancer in the urogenital tract, and 30 per cent of these will be found in the urinary bladder. Complete urologic examination must be done at once to locate and determine the cause of bleeding. Recurrence of bleeding may not occur for several months during which time spread and metastases may occur.

Bimanual palpation (under anesthesia when necessary) will reveal useful information regarding character of tumor and its extension to perivesical structures.

Frequently surgical exploration is necessary to obtain accurate diagnosis of: a) presence of malignancy, b) present extent of local spread, c) presence and extent of abdominal metastases, and to plan and begin the steps incident to radical surgery as diversion of urinary stream and/or cystectomy.

Transurethral operations should be done only for grade 1 malignancy and when no spread or metastases are evident. Radical surgery is immediately indicated if there are local recurrences subsequent to transurethral resection.

When palliative treatment is necessary, diversion of the urinary stream produces more comfort for the patient and permits better control of the local mass.

All tumors of the urinary bladder are malignant. Do away with conservatism and procrastination, and try to cure by early, accurate diagnosis and timely radical surgery.

9622 Brighton Way, Beverly Hills, Calif.

THE JOURNAL OF UROLOGY
Vol 61 No 2 February 1949
Printed in U S A

AMYLOID TUMOR OF THE BLADDER[1]

LYLE G CRAIG

Primary amyloid tumor of the urinary bladder is a distinctly rare condition Apparently only 7 examples are presently found in the literature Of these, 2 are postmortem reports appearing in German publications about fifty years ago, while the remaining 5 clinical cases have all been published in the American literature since 1932 Interestingly enough, 2 of these 5 were described by members of this society, Drs Rusche and Bacon, who in 1941 reported 2 cases from the urological service of the Los Angeles General Hospital My own patient was first seen in January 1942, and has therefore been followed for more than 6 years He was last cystoscoped in March of this year (1948)

CASE REPORT

A white man of 47, married, and the father of 2 children, was first seen on January 8, 1942, because of sudden massive hematuria, so severe as to cause complete urinary retention from clots He had voided normally clear urine the evening before, so the entire duration of symptoms was less than 12 hours There had been no preceding frequency nor dysuria His past history revealed no previous urinary disease and no chronic illness, except that he had been somewhat of an alcoholic, and had also suffered at one time what he called a "nervous breakdown" He appeared to be well nourished and, in spite of the bleeding, was in rather good general condition

He was admitted to the hospital for emergency cystoscopy under spinal anesthesia The general examination was essentially normal, except for the distended urinary bladder The heart and lungs showed no evidence of disease The blood pressure was 135 over 85 The prostate was not enlarged on rectal palpation The initial blood count showed 13 9 gm hemoglobin, or 82 per cent, 4,860,000 erythrocytes, and 13,450 leucocytes, with 74 per cent polymorphonuclears, of which 24 were stab forms The urine obtained through the cystoscope was largely blood The first urinalysis gave a specific gravity of 1 033, pH 7, albumin plus 3, no sugar, hundreds of red cells, and a few white cells Subsequently the serum Wassermann was reported negative and the spinal fluid entirely normal

The cystoscope was introduced easily, the clots were evacuated, and the bladder examined The bladder neck and trigone were entirely normal On the floor of the bladder, back of the trigone and slightly to the right of the midline, was what appeared to be a slightly elevated, flat, infiltrating tumor It was well circumscribed, less than an inch in diameter, and a yellowish-red color The surface was not ulcerated, but blood oozed freely from its anterior margin A tentative diagnosis was made of a malignant tumor and several specimens were taken for biopsy, after which the bleeding was stopped by electrocoagulation

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, British Columbia, April 17, 1948

The sections were examined by Dr. Alvin G. Foord: "Sections show pieces of tissue some of which are covered by stratified epithelium in which there is no evidence of malignancy. In the underlying tissue one sees a bizarre queer-looking stroma in which there are irregular nests of glassy hyaline appearing substance, in which there are only occasional fibroblasts. Here and there one sees a small deposit of calcium. No neoplasm is seen. Congo red stain for amyloid is positive. Frozen sections were stained and show the iodine reaction to be typical, red coloration in methyl violet stains, and a deep red staining by congo red. Diagnosis: Amyloid deposit in the bladder."

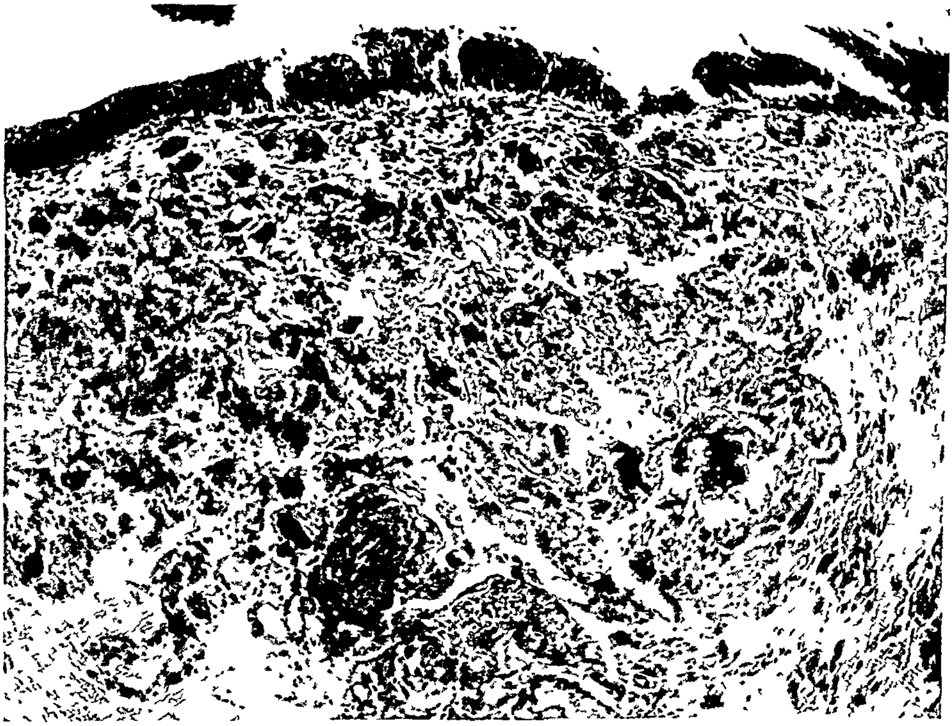


FIG. 1. Normal bladder epithelium with nests of amyloid material deposited in submucosal layer.

Dr. Foord did not arrive at this diagnosis without some difficulty. He was at first confused by the absence of cellular structure, and thought that the lesion was probably a tumor, but that the tissue had been damaged in securing the specimen. Only after some discussion and further study of the material was he able to arrive at the correct diagnosis.

With this positive diagnosis, and the assurance that there was no malignancy, and since the location of the lesion in the floor of the bladder made it unfavorable for resection, it was decided to attempt to destroy it by electrocoagulation, a method that has been used with some success in the treatment of similar solitary deposits of amyloid in the larynx. This was done 5 days later, on January 13, after further biopsy specimens had been taken for confirmation of this rather unusual diagnosis. Retrograde pyelo-ureterograms were also made at this time which were entirely normal.

The electrocoagulation was done transurethrally, but quite thoroughly The convalescence was somewhat stormy, with frequency, burning, and slight hematuria for several days, but practically without fever He was discharged on January 29, three weeks after admission, and his symptoms gradually disappeared He was cystoscoped at intervals of 2 months, and within 6 months the bladder was completely healed Since then he has been examined several times At the last cystoscopy on March 9, 1948, the bladder was entirely normal, without even a visible scar The patient states that he has had no bladder symptoms for years

DISCUSSION

Amyloidosis in the human body, occurring secondary to such chronic wasting disease as tuberculosis or osteomyelitis, is familiar to all of us The name is really a misnomer, originally given because the peculiar blue staining reaction with iodine suggested a chemical relationship to starch The gross appearance and consistency of the material led to the term "lardaceous degeneration", formerly applied to the disease It was first studied thoroughly by Virchow in 1853, and in 1859 Friedreich and Kekule demonstrated the protein nature of the deposits Wells, in his *Chemical Pathology*, accepts the belief that amyloid is a combination of protein with chondroitin sulphuric acid This has, however, been questioned The exact chemical formula appears to vary, and has never been completely established

Amyloidosis is not always secondary to chronic suppurative disease, but occurs in other distinct forms as well In the usual form already mentioned, the most extensive deposits are found in the liver, spleen, and kidneys, which constitutes our familiar conception of amyloidosis However, there is another so-called secondary form associated with, and presumably due to, multiple myeloma, in which the liver and kidneys are nearly always spared and the deposits occur elsewhere, notably in the joints and about the blood vessels

Much less common are the primary types of amyloidosis in which the amyloid deposits may be called idiopathic, since there is no history of preceding or concomitant chronic disease The most common finding is the multiple form, where there are numerous nodules scattered throughout the body, involving especially the mesodermal tissues, the cardiovascular system, the gastro intestinal tract, the smooth and striated muscle, and the lymph nodes Though widely disseminated, it differs from the secondary group in that the liver, spleen, and kidneys may be entirely free This is the more common type of primary amyloidosis

The present patient illustrates the other sub-group, the solitary nodule of primary amyloidosis, the amyloid tumor Shonhof calls this "tumoroid amyloidosis" He objects to the use of the term "amyloid tumor" because he says it carries the suggestion that the nodule is a neoplasm, which it is not These solitary, or occasionally multiple, deposits of amyloid are found most frequently in the larynx or upper respiratory tract, but have been seen in the eye, tongue, pharynx, and genito urinary tract They are never generalized, and are not associated, unless incidentally, with any chronic disease

Very little is really known of the etiology of amyloidosis. Several theories have been advanced to explain the secondary form, but practically nothing has been suggested to account for the primary forms. Even in secondary amyloidosis few experimantal studies have been made, and the mechanisms suggested are largely hypotheses proposed by men reporting clinical cases. A list compiled by Eklund and Reimann includes the following: 1) a general disturbance of protein metabolism; 2) an antigen-antibody union and precipitation; 3) an absorption of protein; 4) a disturbance or abnormality of the reticulo-endothelial system, probably based on the fact that secondary amyloidosis so often involves organs rich in reticulo-endothelial cells; 5) hyperglobulinemia; 6) hyperproteinemia plus some disturbance of the reticulo-endothelial system.

While there may be some evidence in support of each of these theories, none can be considered adequate, and all are distinctly speculative. Moreover, there is little to support any of them as the cause of the primary form of the disease.

The first description of tumoroid amyloidosis in the urinary bladder was an autopsy report by Solomin in 1897. Likewise, Lucksch in 1904 found multiple nodules in a bladder examined post mortem. In 1932 the first clinical case was reported by Chwalla of Vienna, who found and treated a nodule at the margin of the bladder and prostatic urethra, the site of a previous papillary tumor. Nine years later, in 1941, Rusche and Bacon presented 2 patients with this condition from the urology service of the Los Angeles General Hospital. Corbitt, Broders, and Pool, from the Mayo Clinic, in 1944 published the first case in which the diagnosis was made by transurethral biopsy. In 1946, Purcell and Brown, in the Naval Medical Bulletin, described the fifth clinical case. So this patient is the sixth clinical and eighth actual reported case.

The condition does occur elsewhere in the genito-urinary tract. In Chwalla's patient the nodule involved the urethra as well as the bladder. Three other writers, von Tilp, Herxheimer and Reinhart, and von Albertini have also recorded involvement of the urethra. Akimoto found a nodule in the renal pelvis, and Lehmann one in the wall of the ureter. Lubarsch and Winklemann have each reported finding amyloid in the seminal vesicle, and Erken found it in the left testicle.

The one characteristic symptom of all the cases of amyloid tumor of the bladder has been some degree of hematuria. In the patient described by Purcell and Brown, as in this one, bleeding was the only symptom, and was of relatively short duration. In none of the previous patients has it been sudden massive hemorrhage as in this one. The other 4 patients all had frequency and dysuria, doubtless due to the associated secondary infection. In Chwalla's case, where the nodule was in the outlet of the bladder, the chief symptom was obstruction, and the bleeding followed instrumentation. However, bleeding may still be said to be the universal symptom.

The gross cystoscopic appearance of the lesion has not been well described. Purcell and Brown picture a small sessile lesion that had a yellowish edematous appearance and oozed blood. Corbitt, Broders, and Pool saw a "large fungi-form type of growth", and Chwalla described a "solid tumor of uneven surface surrounded by papillary and bullous formations" Rusche and Bacon call it a) "an infiltrating type of tumor", and b) a localized, elevated, irregular, ulcerated, hemorrhagic area" In my patient the area was definitely circumscribed, slightly elevated, distinctly sessile rather than papillary, reddish yellow, not ulcerated, and oozed blood, as described by Purcell and Brown Since with these two exceptions all the patients had advanced lesions with secondary infection, it is probable that this description most accurately pictures the appearance of the uncomplicated deposit, for the slide will show that the pathology is beneath and not in the mucosa Since none of us had any previous experience with the disease, it is natural that in every instance it has been mistaken for a neoplasm, and the proper diagnosis has been made by the pathologist In my own case, and in that reported by Corbitt, Broders and Pool, the specimen was obtained cystoscopically, but in all the others the diagnosis was made after operation by examination of the surgically excised specimen

The differential diagnosis is almost exclusively a matter of distinguishing the deposit from a true tumor, and this will always be a proper function of the pathologist The lesion looks like an infiltrating tumor, though ulceration appears only with secondary infection But the cystoscopist obviously must not trust his visual judgment Cystitis cystica glandularis might easily be confused, and in women the solitary tumor of endometriosis But a well taken biopsy specimen, properly prepared, stained, and interpreted by a competent pathologist, should always lead to the correct diagnosis

The treatment heretofore reported has always been surgical, the lesion being widely excised through a suprapubic approach Four of the writers did segmental resections of the bladder, while Chwalla excised the nodule in the bladder neck and curetted the surrounding area thoroughly Incidentally, he had severe postoperative hemorrhage, so that he was forced to reopen the bladder and pack the bladder neck In my patient the location in the floor of the bladder was not suitable for resection, but was readily accessible to transurethral electrocoagulation This was done very completely, which probably accounts for the slow painful postoperative course It would seem that thorough electrocoagulation should be adequate treatment in the bladder where the mass can be completely destroyed Since there is no element of malignancy, inadequate treatment can be repeated The method has not been entirely satisfactory in the larynx, where the procedure is limited by the delicate nature of the structures and the complications incident to extensive destruction of tissue My patient has been followed for more than 6 years without any evidence of recurrence One of the patients treated by Rusche and Bacon was cystoscoped 4 years after the original treatment and was found to have amyloid deposits remaining in the bladder wall, though without symptoms None of the other patients was observed for any considerable period of time My experience would make it appear that the disease is not a fatal one, and that the chief hazard lies in the probability of repeated bleeding

The histological picture is well shown The mucous membrane is intact and the amyloid is deposited in the submucosal layer and between the muscle fibres. This was noted also by Purcell and Brown. Secondary infection with ulceration later becomes an important part of the clinical picture. Congo red stain gives the characteristic red color, which also occurs in vivo. The deposits are also stained red by methyl violet and blue with iodine, which further identifies them as amyloid.

65 N. Madison Ave., Pasadena 1, Calif.

REFERENCES

Chwalla, R.: Case of amyloidosis at bladder neck resembling a tumor. Urol. & Cutan. Rev., **36**: 381–384, 1932.

Corbitt, R. W., Broders, A. C. and Pool, T. L.: Amyloidosis of the bladder. J. Urol., **52**: 153–157, 1944.

Eklund, C. M. and Reimann, H. A.: The etiology of amyloid disease. Arch. Path., **21**: 1–9, 1936.

Lucksch: Ueber locale Amyloidbildung in der Harnblasse. Verhandl. d. deutsch. path. Gesellsch., **7**: 34–39, 1904.

Purcell, H. M. and Brown, C. E.: Amyloid tumor of the bladder. Naval Medical Bull., **48**: 1607–1610, 1946.

Reimann, H. A., Koucky, R. F. and Eklund, C. M.: Primary amyloidosis limited to tissue of mesodermal origin. Am. J. Path., **11**: 977–988, 1935.

Rusche, C. F. and Bacon, S. K.: Solitary tumor-like amyloidosis of the urinary bladder. Trans. Am. Assoc. Genito-Urin. Surg., **34**: 163–168, 1941.

Solomin, P.: Ueber locales circumscripted Amyloid in der Harnblasse. Prag med. Wchnschr., **22**: 3–5, 1897.

Wells, H. G.: Chemical Pathology. Philadelphia: W. B. Saunders Co., 4th ed., 1920, pp. 421–427.

THE JOURNAL OF UROLOGY
Vol 61, No 2 February 1949
Printed in U S A

PRACTICAL CONSIDERATIONS IN THE USE OF HIGH FREQUENCY CURRENTS FOR TRANSURETHRAL PROSTATECTOMY[1] [2]

HENRY M WEYRAUCH, J BRANDON BASSETT AND MAX M BERGER

From Department of Urology, U S Veterans' Administration Hospital, Fort Miley, San Francisco, Calif

Since 1882 when d'Arsonval introduced the use of a low frequency sine wave current for fulguration, numerous investigators have further developed and modified electrical currents for use in surgical procedures In modern electrosurgical units, currents with frequencies of several million waves per second are produced These frequencies are employed solely to insure the safe passage of electrical energy through the living body without eliciting other than electrosurgical effects in the region of the active electrode

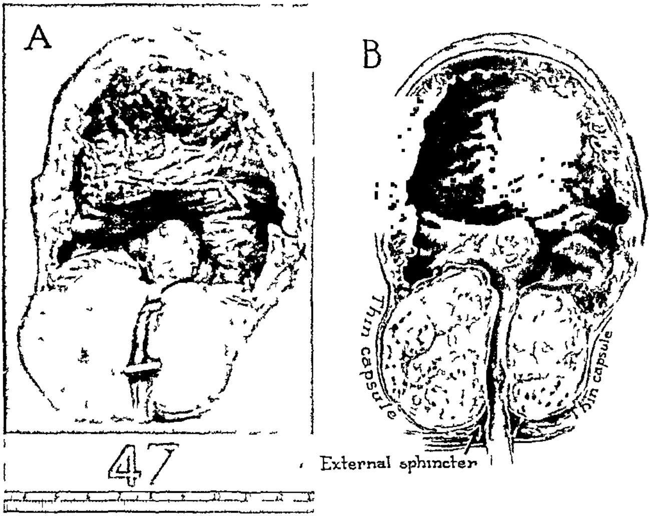


FIG 1 *A*, Actual specimen *B*, Diagram showing how large hypertrophies produce marked thinning of prostatic capsule and bulge into urogenital diaphragm around external urinary sphincter

Caulk and Patton found that high frequency currents, similar to those generated by modern units, produced elevations of temperature exceeding the thermal death point 2 cm. from the active electrode. Yet Flocks, in observing healing of the prostatic fossa subsequent to transurethral prostatic resection, stated that destruction of tissue did not extend beyond a depth of 3 to 4 mm.

---

[1] Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans' Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors

[2] Read at annual meeting, Western Section, American Urological Association, Victoria, B C, April 21, 1948

When our present day operative technique entails the resection of prostatic hypertrophy down to an attenuated capsule which may be no more than a few millimeters in thickness, and when resection at the apex may approach to within a few millimeters of the external urinary sphincter (fig. 1), it is essential to know the exact inherent potential dangers of each type of current. We have made investigations in order to gain a precise conception of these dangers.

Wounds made with high frequency currents differ from those made with a scalpel in that they produce a surrounding zone of devitalized tissue. When this occurs in the prostatic fossa, healing takes place by the separation of slough, the development of granulation tissue and eventual epithelialization. The narrower the zone of devitalized tissue, the smaller is the foothold for infection and the more quickly healing takes place. The devitalized zone is caused by heat generated in tissue from electrical forces concentrated in the vicinity of the active electrode. When sufficient heat is generated, the thermal death point is reached and a zone of devitalized tissue produced.

METHOD

Factors causing the zone of devitalized tissue have been studied by two methods: 1) by determining the rise of temperature in the area surrounding the active electrode; 2) by observing the gross changes which immediately result.

Preliminary experimentation proved that we could make better observations in isolated tissue than under actual operating conditions. Comparison of prostate, seminal vesicle, kidney, liver, muscle, fat and fascia showed that fresh liver closely approximates prostatic tissue in its response to high frequency currents and is admirably adapted to portraying gross changes.

For tissue, we used fresh liver kept at body temperature prior to and during the experiments. Cutting and coagulating were performed with a Stern-McCarthy electrotome, in an artificial bladder, through which a stream of water was passed. Currents from latest models of spark gap and tube electrosurgical units were used to activate a loop 0.012 inch in diameter (except in the series performed to evaluate the size of the electrode). Additional observations were made of thermal effects during actual operating conditions.

Thermal effects were studied with the use of a thermocouple (fig. 2). With the aid of a trocar, a specially constructed thermopile was inserted to the desired depth in the liver, the experiment performed, the tissue sectioned and the position of the thermopile checked. Frequently, despite meticulous care, the thermopile was found to be located a few millimeters distant from the site determined by surface measurements, making repeated placing of the thermopile necessary. The impracticability of accurate determination of thermal effects during actual operation is thus readily understandable. Because of this difficulty we made no attempt to insert a thermopile into the prostate through the perineum, but we did make a rough check on our experimental findings by placing a thermopile against the rectal surface of the prostate during resection.

Since urologists refer to current densities produced by electrosurgical units in terms of dial settings, we report such current values simply as "dial settings" as found on commercial units. There are constantly changing variables, such as variation in the resistance of tissue, the characteristics of the active electrode, and surges in the line output, which make it difficult to determine accurately the current values during each step of the operation An increase in the dial setting does not affect the frequency, but increases the intensity of the current as can be expressed by a higher wattage

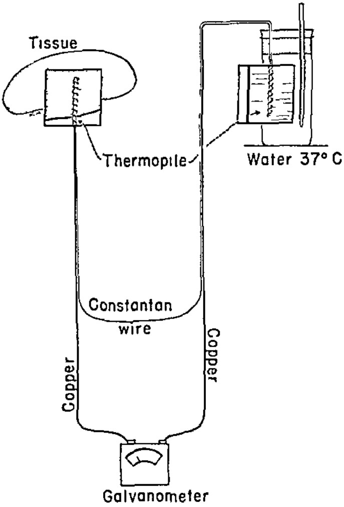


FIG 2 Thermocouple used in experiments

THERMAL EFFECTS

The physiological death point of human tissue is attained by temperatures of or exceeding 45 to 47 degrees centigrade.

In measuring elevations of temperature in tissue produced by coagulating currents, we varied the time of application of the active electrode and the current density as indicated by the dial setting

During 10 seconds' application of the active electrode, using a dial setting of 30 on the spark gap unit, the zone at which the thermal death point of tissue was reached was confined within a radius of 3 mm (fig 3). Following a 32 C rise at 2 mm., there was a rapid drop in the temperature out to 1 5 cm. beyond which no thermal effects were noted. Similar tests with a tube coagulating current showed an even smaller radius of thermal effects. By increasing the dial setting to 60, the radius of the thermal death point extended out to 4 mm. with the spark gap current, the thermal rise tapering off at 2 cm. The rise from a corresponding tube coagulation current was lower.

In observing the effect of the time of application of coagulating currents, at a dial setting of 30 at a distance of 3 mm. between the thermopile and the active electrode, we noted a prompt rise in temperature during the initial 6 to 8 seconds of application of the active electrode, following which there was little further increase in elevation (fig. 4). At no time was the thermal death point reached at this distance. Similar curves of temperature elevations were produced at higher intensities if the thermopile was placed outside the zone of the thermal death point. These findings were corroborated by the depth of zones of coagulation produced in tissue.

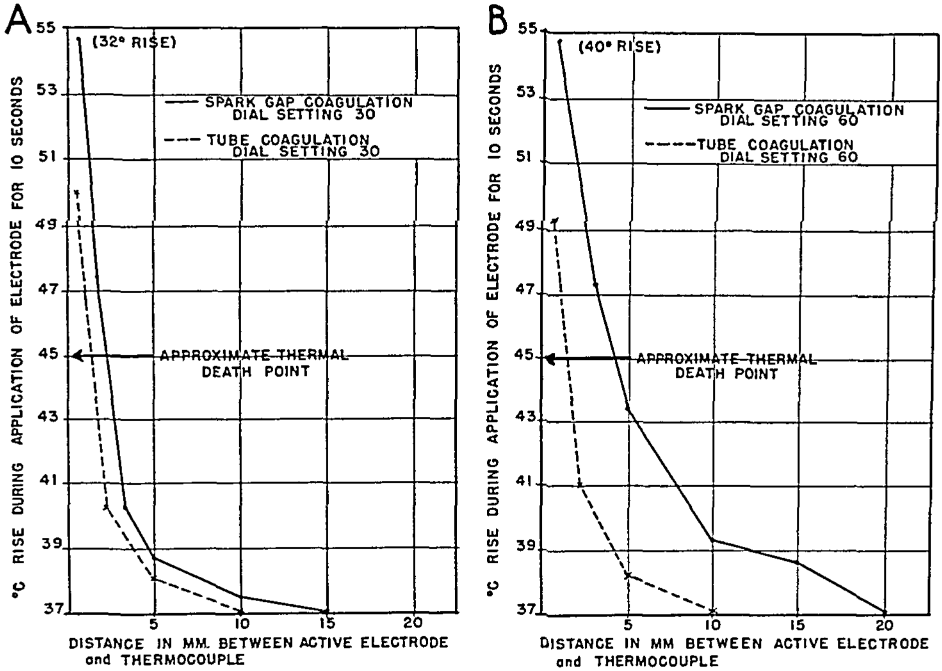


FIG. 3. Elevations of temperature produced by coagulating currents at various distances from active electrode. *A*, During single 10 second application of electrode at dial setting of 30, thermal death point is exceeded at 2 mm. but is not attained at 3 mm. *B*, At dial setting of 60, rise to thermal point extends out to 4 mm., but is not exceeded at 5 mm. Rise from a tube coagulation current is slightly lower than for spark gap current.

With the exception of the time of application, similar variables were employed in considering the thermal effects of cutting currents. Temperature elevations were recorded at the maximal rise produced by the moving electrode as it resected tissue over the thermopile. It is impossible to maintain contact of the electrode at any given point as with the coagulating electrode, since the tissue retracts and loses contact with the loop as soon as it is cut. If the loop is advanced, to maintain contact, the distance between the loop and the thermopile is no longer constant.

Using a current density as indicated by a dial setting of 60 there was no obvious rise of temperature beyond 1 cm. from the advancing loop (fig. 5, *A*). Upon increasing the dial setting to 100, the outer limit of observable temperature

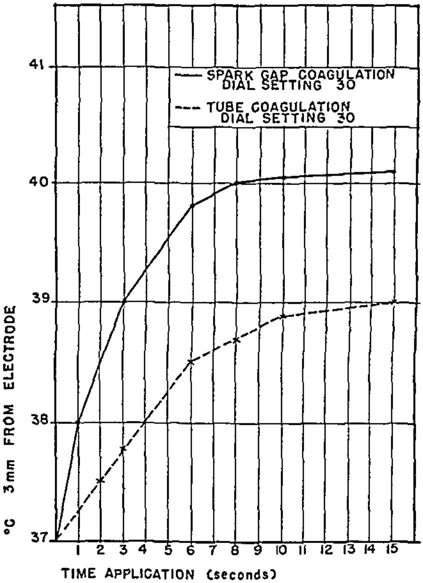


Fig 4 Effect of time of application of electrode activated by coagulating currents at dial setting of 30 At distance of 3 mm thermal death point is not exceeded up to periods of application of as long as 15 seconds Maximum rise is attained during first 6 seconds of application, after which curve tapers off

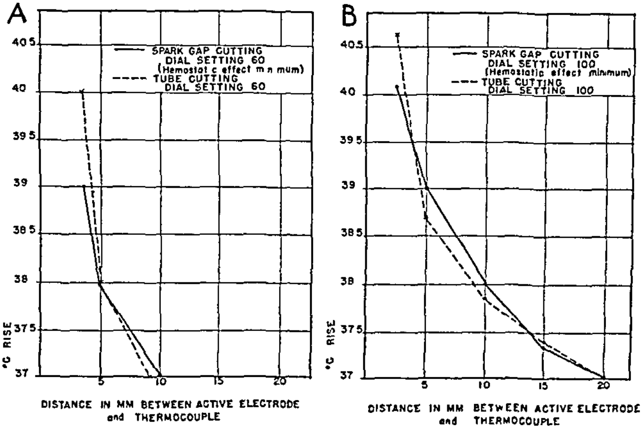


Fig 5 Elevations of temperature produced by cutting currents at varied distances from active electrode *A*, With dial setting of 60 there is no rise beyond 1 cm *B*, At 100 there is no rise beyond 2 cm In neither instance does elevation exceed thermal death point of tissue beyond a radius of 3 mm

change extended to 2 cm. (fig. 5, *B*). The elevation of temperature did not exceed the thermal death point beyond a radius of 3 mm. from the loop, regardless of the current intensity or the speed of cutting. There were no appreciable differences in the elevation of temperature between the tube and spark gap units using comparable dial settings.

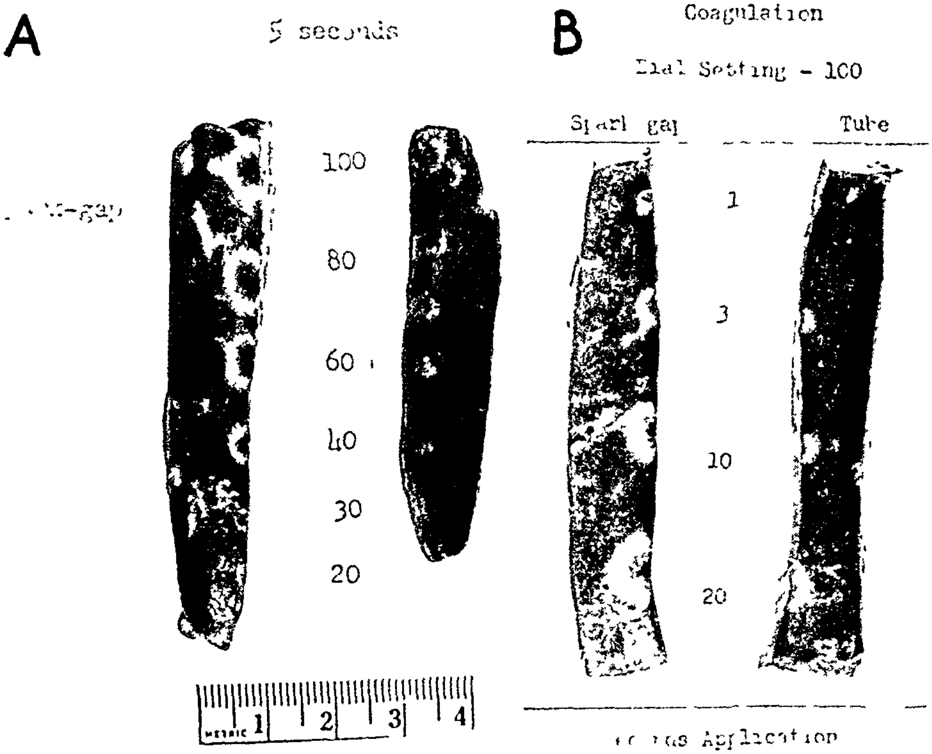


FIG. 6. *A*, Effect of intensity of coagulating currents on radius of zone of coagulation Single 5 second applications of electrode. Numerals indicate dial settings. Coagulated zones on left were produced by spark gap unit, those on right by tube unit. Gross tissue destruction from point of application is measured as follows:

Dial setting	*Spark gap* *mm*	*Tube* *mm*
100	7	3
80	6	2
60	5	2
40	3	1
30	2	0.5
20	1	—

B, Effect of time of coagulation on zone of tissue destruction. Dial setting maintained at 100 while varying time of coagulation. Longer the time of application, wider is zone of coagulation. Spark gap current produces more gross tissue destruction than tube.

GROSS TISSUE CHANGES

Gross changes of tissue were observed as a change in color in coagulated zones and by evidence of surface charring.

Coagulated zones were first produced in liver by 5-second applications of the active electrode, varying the intensity of the coagulating currents delivered by the spark gap and tube units (fig. 6, *A*). It was found that the zone of tissue

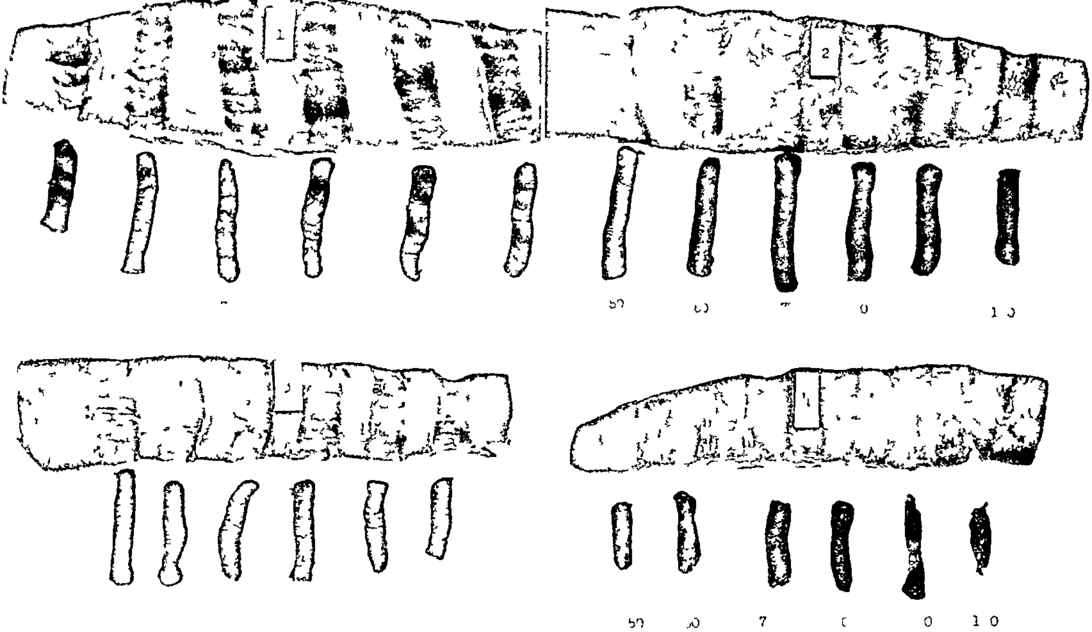


Fig. 7. Effect of cutting speed and comparison of spark gap and tube cutting currents in producing surface charring. *1*, Slow strokes taken with spark gap current. There is pronounced charring and narrow zone of coagulation at edges of furrows, slightly more evident with higher dial settings. *2*, Fast strokes taken with spark gap current. There is absence of any marked degree of surface charring except for slight intensification in two highest dial settings. *3*, Slow strokes taken with tube current. There is a narrow zone of coagulation on either side of furrows and a small degree of surface charring with higher dial settings. These changes are less marked than with spark gap current. *4*, Fast strokes taken with tube current. There is practically complete absence of any apparent gross surface charring.

destruction was directly proportional to the intensity of the current. With a dial setting of 30 on the spark gap unit the radius of coagulated tissue was 1 mm., increasing proportionately to 7 mm. at the maximum dial setting of 100. The tube current produced a 0.5 mm. radius of coagulated tissue at 30, increasing to a zone of 3 mm. at 100.

Confirming previous observations with the thermocouple, varying the time of application while keeping the intensity of the current constant, it was found that with lower dial settings (at 30 for the spark gap coagulation current) the zone of coagulated tissue was defined within the first 6 to 8 seconds, after which prolonged application up to 15 seconds or more produced little increase in the coagulated area. Sections of tissue showing the zone of coagulation from less intense currents demonstrate little difference in the size of the coagulated zone from 6 to 15 seconds. The more intense currents show a progressive increase in the size of the zones of coagulation, continuing beyond 20 seconds, at which point the experiment was concluded (fig. 6, *B*).

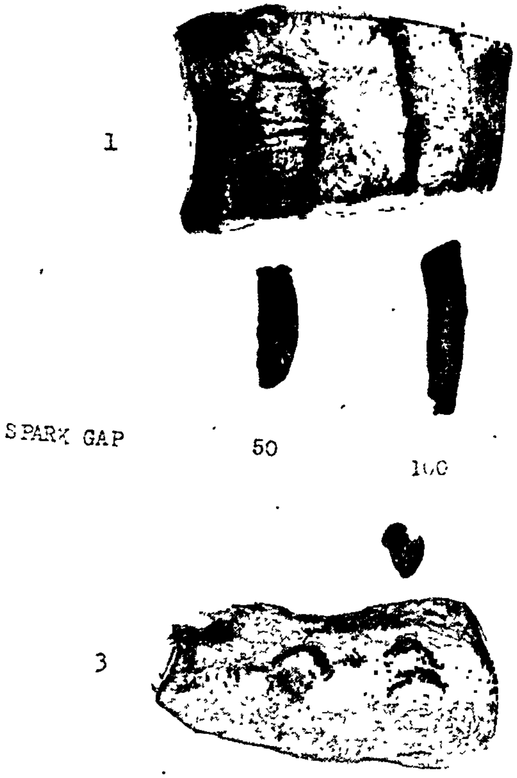


FIG. 8. Effect of increasing hemostatic element in blended spark gap current. *1*, Hemostatic effect at minimum (dial setting 1) using slow cutting stroke at dial setting 50 and rapid stroke at 100. *3*, Hemostatic effect increased to dial setting of 3. Attempt at cutting at 50 and 100 is unsuccessful.

Cutting currents do not produce zones of coagulation such as are observed with coagulating currents because an electrode activated by a cutting current does not maintain contact with the tissue. Devitalized tissue, produced by a cutting current, is evidenced by a thin crust of desiccated tissue which shades brown to black in color; the deeper the color the greater the destruction of tissue. This superficial crust is best described by the term "surface charring."

The effects of varying the speed of cutting and the intensity of the current were observed. Strokes completed in less than ½ second for the excursion of the loop were defined as "rapid" strokes; "slow" strokes required 2 seconds. At any given density of current, less charring was produced with a rapid stroke. A rapid stroke made at a maximal dial setting of 100 produces less damage than a slow stroke at a dial setting of 50, the factor of current intensity being of much less consequence than the speed of cutting (fig. 7).

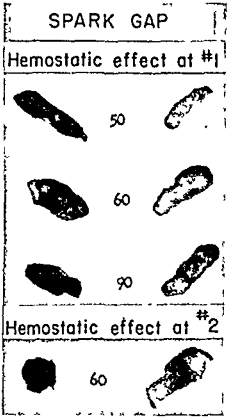


FIG. 9. Effect of cutting speed and hemostatic element in producing surface charring Resected sections of prostatic tissue showing that slow excursion of loop (sections on left produce more surface charring than rapid cut (sections on right) and that higher the proportion of coagulation effect in a blended current, greater is surface charring. Note black crust on all sections to left as compared with light grey surface of sections to right.

Of the two types of current, it was noted that the tube unit produced less surface charring. This is accounted for by the fact that the spark gap cutting current is of the blended type, incorporating a small element of coagulating current even at a minimal dial setting of 1. Increasing the coagulation effect by advancing the dial setting to 2 or more, produced not only more surface charring, but reduced the cutting efficiency of the current. Thus, even with a maximum cutting intensity (dial setting 100) and the hemostatic effect increased to 3, it was impossible to make a smooth, uninterrupted furrow (fig. 8).

OBSERVATIONS DURING OPERATION

During transurethral prostatectomy, with the resection loop approaching the posterior prostatic capsule, no temperature elevation was recorded by the thermopile in the rectum when separated from the active electrode by an estimated thickness of tissue of 1 cm., even during periods of coagulation up to 5 seconds with a dial setting of 50 on the spark gap unit. Similarly, using a cutting current, with a dial setting of 60, there was no elevation of temperature with either tube or spark gap units.

Tissue fragments obtained during actual resection again showed that the major factor causing surface charring is cutting speed, and, to a lesser degree, intensity of current (fig. 9).

ADDITIONAL FACTORS

Additional factors of importance in the use of high frequency currents are: the size of the active electrode, the moisture content of the tissue, and the cumulative effect of rises in temperature in the tissues as evaluated by the dispersion of heat into the irrigating medium.

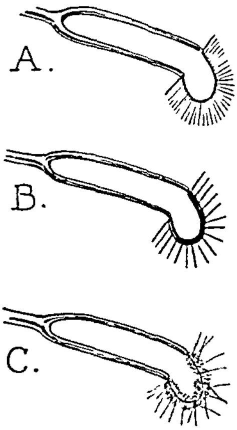


FIG. 10. Effect of size and incrustation of loop—active electrode. *A*, Thin loop. *B*, Thick loop. *C*, Incrusted loop. Diagram illustrates how diameter of wire forming loop affects intensity of current entering tissues. All loops are transmitting same amount of current. The thinner the loop, more concentrated is current. The thicker the loop, more current is required for same degree of efficiency and wider zone of destruction. Coagulated tissue which remains adherent to loop increases its diameter and also causes dispersion of current. Lower the conductivity of incrusted material, the less current is transmitted. Incrustation is a greater factor than size of loop.

When the diameter of wire forming the active electrode is small, the electrical waves are more concentrated and give greater cutting efficiency (fig. 10). Utilizing the same intensity of current, a wire of larger caliber or incrusted with carbonized tissue has impaired cutting quality. This inefficiency is caused by greater dispersion of the electric waves. We demonstrated that a loop formed of wire 0.012 inch diameter cuts fresh liver at a dial setting of 50, a 0.015 inch wire loop requires a dial setting of 60 before cutting identical tissue, whereas an incrusted 0.012 inch wire loop requires a dial setting of 70.

Cutting efficiency was directly proportional to the moisture content of the tissue. Charred surfaces and surfaces dried by prolonged exposure to air cut with difficulty.

Observations were made of the dispersion of heat into the irrigating medium so as to evaluate the cumulative effect of thermal rises as contrasted with the more localized destructive effects at the site of the electrode. This could not be readily estimated when using a flowing current of large quantities of water (capacity of artificial bladder was 400 cc) which made the factor of dispersion so great that no significant rise of temperature (less than 1 C) was noted in the preceding experiments

However, by modifying the experimental conditions, we were able to study the elevation of temperature produced in the water medium by the various currents We used pieces of liver, weighing 30 gm , immersed in 60 cc water which was constantly stirred, but not changed, during the experiment Cutting and coagulating currents were used, keeping the loop in slow motion so as to maintain contact with the tissue during the cutting strokes, and to avoid the insulating effect of desiccated tissue while coagulating

TABLE 1 *Rise of temperature (degrees centigrade) in water medium, applying various high frequency currents to 30 gm of liver in 60 cc water*

TYPE OF CURRENT	DIAL SETTING	30 SECONDS		60 SECONDS	
		Spark gap	Tube	Spark gap	Tube
Coagulation	30	3°	0	6°	1°
Coagulation	60	5°	1°	12°	2°
Coagulation	100	7°	2 5°	15°	10°
Cutting	60	1 5°	4°	3°	15°
Cutting	100	5°	9°	12°	18°

With both types of current there was a gradual rise in the temperature of the water medium, directly proportional to the time of application and to the intensity of the current (table 1)

During prolonged use at higher dial settings, rises of temperature were observed up to 18 C , well into the thermal death range

CONCLUSIONS

Theoretically, the results of our experiments are capable of close clinical application Since living tissues are subject to the constant cooling effect of circulating vascular elements, even less damage may be expected during actual operation, and the zones of devitalized tissue observed experimentally should not be exceeded during operation

Results show that coagulating currents are the most destructive and must be used with special care While a coagulating current produced by a dial setting of 30 caused no damage beyond a radius of 3 mm , during periods of application as long as 15 seconds, the use of higher dial settings caused progressively wider zones of destruction even during short intervals of time The radius of the zone of destruction is proportionate to the intensity of the current and the length of time of application The more intense the current and the longer the period of application, the greater is the danger of immediate or delayed perforation when coagulation is carried out in the vicinity of the prostatic capsule, and the greater is the hazard of urinary incontinence when it is carried out near the external urinary sphincter

Therefore, in utilizing a coagulating current, it is essential to maintain as low an intensity as possible, with a dial setting of about 30. With low intensity, after the first few seconds, the zone of coagulated tissue is defined and further progress is hindered by the insulating effect of the desiccated tissue and the increased distance from the electrode. The more intense the coagulating current, the wider will be the zone of coagulation, and the more extensive the zone becomes during prolonged application.

The spark gap coagulating current produces more destruction of tissue than a tube coagulating current. Therefore, one might deduce that the tube coagulating current is more desirable; but we know from clinical experience that this is not true. The spark gap current far surpasses the tube current in speed and efficiency of coagulation. Employing proper precautions, therefore, a spark gap current is preferable for coagulation. Exact point coagulation should be used to limit destruction of tissue as much as possible and to prevent the formation of a crust which compromises further cutting.

Cutting currents are not so destructive and do not give rise to zones of coagulation as are observed with coagulating currents. This is largely due to the fact that an electrode activated by this type of current does not maintain contact with the tissue. As the loop is advanced, a fissure is formed and the adjacent tissue retracts in its wake. Devitalized tissue, produced by a cutting current, is evidenced by surface charring. Under ideal conditions there is no gross evidence of surface charring.

With regard to damage caused by cutting currents, no destruction of tissue will result beyond a radius of 3 mm. from the loop, regardless of the type or intensity of the current, or the speed of the cutting stroke. The destruction of tissue within this zone can be kept to a minimum by using a rapid cutting stroke, assured by a current of sufficient intensity. Increasing the intensity of a cutting current does not appreciably widen the danger zone as occurs with coagulating currents. In addition to shortening the time of operation, a rapid cutting stroke prevents charred tissue from adhering to the loop and eliminates the occurrence of tags and frayed edges. Any appreciable increase in the hemostatic effect of a blended current impairs cutting efficiency and is to be avoided.

Results in cutting indicate that tube current is more efficient than spark gap current, and causes less surface charring. It is more satisfactory to use for cutting purposes, although in vascular glands a blended current with a minimum hemostatic effect may be accompanied by less bleeding.

Other factors of importance are: 1) the size of the active electrode; 2) the moisture content of the tissue; 3) the dispersion of heat into the irrigating medium.

The smaller the diameter of the loop, the more concentrated are the electrical waves, and the greater its cutting efficiency. Utilizing the same intensity of current, a loop which has a large caliber or is incrusted with carbonized tissue will be found to have impaired cutting qualities due to greater dispersion of the electric waves.

Cutting is more readily accomplished in tissue with a higher moisture content. When the tissue is dry, as in a fibrous gland, or when extensive coagulation has been carried out, cutting may be difficult, and only made possible by using a loop of small caliber which is activated by a current of high intensity.

Regarding the cumulative rise of temperature in tissue, as measured by its dispersion into the irrigating medium, cutting currents caused as significant a rise as coagulating currents. Since cutting currents are the less dangerous under appropriate operating conditions, one might suspect that they produce a lesser emanation of heat. However, the explanation for this apparent discrepancy is obvious. Whereas coagulating currents maintain contact with the tissue and concentrate their thermal effects at one point, the equivalent thermal effects of a cutting current are widely dispersed over the broad expanse of a furrow. This series of experiments demonstrates the importance of a sufficient flow of a cold irrigating medium during operation. Temperature rises, felt by a finger in the rectum, when noted during prostatic resection, should be considered a danger sign indicating that there is insufficient flow or volume of the irrigating medium.

SUMMARY

It is apparent that the closer the modern operation for transurethral prostatectomy approaches perfection, the greater are the hazards encountered.

In evaluating the various types of high frequency currents used in electroresection of the prostate, the factors responsible for the destruction of tissue were studied by two methods: 1) by determining the rise of temperature in the area surrounding the active electrode; 2) by observing the gross changes which immediately result.

Coagulating currents are the more destructive and potentially dangerous. Therefore, they should be of as low intensity as practicable. In using current of low intensity for point application, the danger is minimal and the factor of prolonged application may be discounted.

In employing cutting currents, the cutting stroke should be as rapid as possible, using a loop of small caliber and as intense a current as is required for rapid cutting. The use of cutting currents of high intensity adds little to the danger of the procedure while contributing a great deal to operating facility.

When applied to electroresection of the prostate, the spark gap coagulating current is far superior to that developed by a tube unit. Provided the hemostatic effect of the blended spark gap current is kept at a minimum, there is not much difference between the two types of cutting currents. However, under most circumstances a pure unblended tube current is more desirable.

Other factors considered are the size and incrustation of the active electrode, the moisture content of tissue, and the cumulative effect of rises in the temperature of the tissues as evaluated by the dispersion of heat into the irrigating medium.

384 Post St., San Francisco, Calif.

REFERENCES

[illegible] J.: Characteristics of adequate electro-surgical current. [illegible] 1932.

[illegible] Influence of type of current on postoperative complications in transurethral surgery. J. A. M. A., 102: 117–123, 1934.

Flocks, R. H.: Local repair following transurethral prostatic resection: Its role in the clinical events associated with this operation. J. Urol., 40: 208–232, 1938.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

CONGENITAL ANOMALIES OF THE DUCTUS DEFERENS AND EPIDIDYMIS[1]

LEWIS MICHELSON

Congenital abnormalities of the ductus deferens and epididymis are not so uncommon as the relatively few cases reported in the literature would lead us to believe. That I have found 12 such abnormalities out of approximately 900 subfertile men (about $1\frac{1}{3}$ per cent) and that R. S. Hotchkiss has had about 20 and F. A. Simmons about 8 (with about the same percentage) not hitherto published, indicates the comparatively common occurrence of these abnormalities that are not recorded in the literature. All of the patients examined by me were apparently normal except for the genital defects. However, one of them showed defects of some of the calyces of the left kidney. In the usual routine examination of a patient it is extremely doubtful if the anomalies would have been recognized.

In a study of 74 cases collected from the literature the following abnormalities were noted: There were 53 cases of aberrant vasa (47 unilateral, 6 bilateral); 20 cases of absence of the vas (18 unilateral, 2 bilateral); in one other case unilateral absence of the vas occurred with aberrancy of the opposite vas. Defects of the epididymides occurred in association with defects of the vasa in 60 of the cases; aberrant epididymis in 40 cases (37 unilateral, 3 bilateral); absent epididymis in 20 cases (18 unilateral, 2 bilateral). In 10 cases information concerning the epididymis was lacking.

Anomalies of the vaso-epididymal system usually occur in association with congenital maldevelopment of the testis and not infrequently with that of the urinary tract. Of the 74 collected cases, defects of the testes were present in 58 patients. Both testes were congenitally absent in 5 cases and one was absent in 23. Unilateral cryptorchid occurred in 30 cases. (No bilateral undescended testicle with defect of the epididymis or vas was recorded.) One apparently aberrant vas and epididymis was noted at operation following a previous orchipexy (Wangensteen). Defects of the uropoietic system were noted in 20 cases. Incomplete reports in many of the autopsy cases and obviously incomplete examination of the urinary tract in most patients operated on prevent the obtaining of satisfactory figures.

Bilateral normal testes were reported in only 16 of the 74 collected cases. Priesel reported 10 cases of normal testes with various anomalies of the genital system, associated in 9 cases with defects of the uropoietic system, Brack 2 cases, Verocay and Anspenger each 1 case. Guizzetti recorded 1 case in which the development of the urinary tract was normal. Recently Mathé reported a case with double right vas deferens and absent right kidney.

In 8 of Priesel's cases there was absence of the vas, portions of the epididymis, seminal vesicle, ejaculatory duct, kidney and ureter of the same side. In 3 of these, defects of the bladder on this side were recorded In the ninth case unilateral absence only of the vas, epididymis, seminal vesicle and ejaculatory duct was noted The tenth case (Priesel) is the only case found in the literature in which both testicles were normal with bilateral absence of the vas The body and tail of the epididymis, seminal vesicle and ejaculatory duct were likewise absent on both sides The right kidney and ureter were absent. There was a left pelvic kidney with a short ureter

---

[1] Read at annual meeting, Western Section, American Urological Association, April 20, 1948.

I am reporting 11 cases with absence of the scrotal portion of both vasa and normal testes in the scrotum Priesel's tenth case is the only one recorded in the literature with similar findings in these organs In my twelfth case only the left vas was absent, the right vas and both testes being normal

CASE REPORTS

Cases Operated On

Case 1 (table 1, fig 1) Bilateral absence of the vas in the scrotum, aberrant epididymides, normal testes

A well developed, normal appearing man, aged 29 years, had normal distribution of hair The genitals were the only organs in which abnormalities were noted The penis was normal Both testes appeared normal and were situated in the scrotum The globus major and body of the epididymides of both sides were present Neither the globus minor nor ductus deferens could be palpated on either side The prostate and seminal vesicles were apparently normal. Examination of the semen demonstrated no spermatozoa The amount was greatly decreased (1 0 cc) Tissue from both testes obtained by biopsy was grossly and microscopically normal Exploratory operation: Both testicles were normal The globus major and corpus of the epididymides on both sides were present but the tubule was greatly dilated On the right these parts were not so large as those on the left. There was bilateral absence of the globus minor. The yellow, pus-like material that exuded on puncture of the body was odorless and contained great numbers of tailless spermatozoa, some spermatogenic cells and minute, faint, yellow appearing cubic crystals Few pus cells were evident No evidence of either vas could be discovered

Case 2 (table 1) Bilateral absence of vas in scrotum, congenitally normal epididymides and testes

The physical findings were similar to case 1 except that both epididymides appeared congenitally normal The patient was 26 years old The tissue obtained from both testes was normal No spermatozoa were present in the semen Exploratory operation (permitted only on one side): A normal left testis and congenitally normal epididymis were found The tubule was distended and upon puncture a yellow-brown purulent material was extruded Microscopically many tailless heads were seen No vestige of the vas could be discovered

Case 3 (fig 2) Left Congenital absence of vas in scrotum, aberrant epididymis Right Normal epididymis, acquired obstruction of normal vas Both testes normal

In a patient aged 33 years the past history was negative except for gonococcal epididymitis The patient did not remember whether it had occurred unilaterally or bilaterally. The only physical abnormalities were in the genitals. The penis and both testes appeared normal. The right epididymis was harder and firmer than normal. The globus minor was enlarged and hard. The left epididymis appeared normal in size. The body was harder than normal. The right vas was present and appeared normal. No vas could be demonstrated on the left.

TABLE 1. *Bilateral congenital absence of ductus deferens in scrotum, normal testes in scrotum, azoospermia*

CASE NO	AGE	TESTES		EPIDIDYMIS		PROSTATE SEM. VES.	OTHER ABNORMALITIES	SEMEN VOL. CC
		Phys. Exam.	Biopsy	Right	Left	Phys. Exam.		
				Operated cases				
1	29	Normal	Normal	Aberrant	Aberrant	Normal	—	1.0
2	26	Normal	Normal	Normal	Normal	Normal	—	—
				Nonoperated cases				
4	29	Normal	—	Aberrant	Aberrant	Normal	—	0.5
5	28	Normal	Normal	Normal	Normal	Small prostate Sem. ves. norm.	—	0.5
6	32	Unequal size normal	—	Normal	Normal	Normal	—	0.5
7	28	Normal	—	Normal	Normal	Normal	Projecting mass into intervesicular notch	0.75
8	21	Normal	—	Absent	Absent	Normal	—	1.0
9	31	Normal	Normal	Normal	Normal	Normal	—	1.0
10	25	Normal	Normal	Normal	Normal	Normal	Abnormal left kidney	1.5
11	26	Normal	—	Normal	Normal	Normal	—	1.5
12	31*	Left normal Right globular	—	Right g. major cyst	Normal	Normal	—	—

* No specimen of semen.

The prostate and seminal vesicles appeared normal on palpation. The secretion expressed by "massage" was normal. No spermatozoa were present in the semen; there was 2.5 cc in quantity. Bilateral biopsies demonstrated normal testicular tissue. Operation (right vaso-epididymostomy, left exploratory): Left:—Testis normal. No vas or vestige of one could be found (fig. 2). Epididymis about $\frac{1}{2}$ to $\frac{2}{3}$ normal length, ending in a small nubbin. The globus

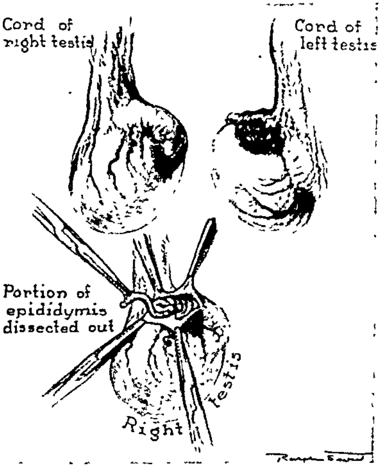


FIG. 1. Case 1. Normal testes and globi majoris. Small corpus. Absence of globi minoris and vasa.

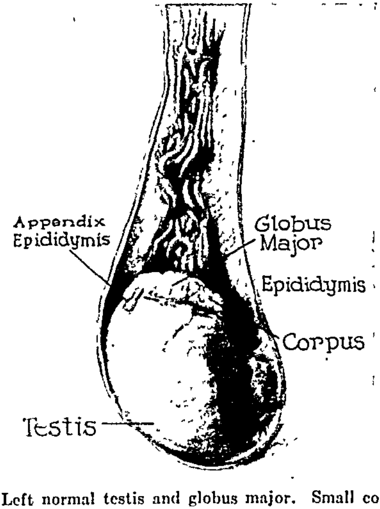


FIG. 2. Case 3. Left normal testis and globus major. Small corpus. Globus minor and vas absent.

major was present but it could not be decided if the body ended in the blunt nubbin or if this was part of a small globus minor. The lumen was distended and upon puncturing it yellow, purulent material was extruded. This showed many completely normal shaped amotile spermatozoa. (Slides lost in operating room, therefore a complete microscopical examination not made.)

Right:—Evidence of the previous inflammatory disease in the form of old adhesions were present between the layers of the tunica. Normal testis. Globus major felt hard and fibrous. No secretion upon incising the tubule. (Post-operatively active spermatozoa were present in the ejaculated semen.) The corpus appeared normal; the globus minor thickened and hard. The vas felt normal and distal lumen patent beginning 2.0 cm. to 3.0 cm. from the epididymis. Successful vaso-epididymostomy.

Non-operated Cases (Table 1) Cases 4–12

In 8 cases the diagnosis of normal testes, bilateral absence of the ductus deferens and normal, aberrant or absent epididymis was based on the history, physical examination and semen analyses. In the ninth case a semen specimen was not obtained. In 3 of these cases (Nos. 5, 9, 10) biopsies confirmed the diagnosis of normal testes. In all cases the prostate and seminal vesicles were normal per rectal examination.

In 1 case (No. 6) both testes had apparently been normal up to an attack of mumps orchitis at 20 years of age. Following this the right had atrophied. The left appeared normal. It was deemed justifiable to include this as a case of congenitally normal testes.

Both epididymides were absent in 1 case (No. 8) and aberrant in 1 (No. 4). In case 12 the right globus major was enlarged and cystic, the left being normal. No semen specimen was brought in for examination. In only 1 case (No. 7) was an abnormality noted on physical examination that apparently involved an internal structure developed from the wolffian duct. This mass was felt projecting into the intervesicular notch above the prostate and apparently between the rectal wall and trigone of the bladder. It was firm and fixed in position but not hard or tender. The lower end was rounded and estimated to be about 2.0 cm. in diameter. The upper border could not be determined; however, the length of the abnormality was over 4.0 cm. The diameter had gradually and symmetrically increased to about 3.0 cm. at this distance. Urograms from this and one other case (No. 1) showed bilateral normal kidneys. Urograms were obtained in only one other case (No. 1) and showed deformities of the upper, lower and middle calyces of the left kidney. The contour and size of both kidneys were normal. The defects of the vasa in case 11 differed from those of the rest of the group in that the portion of the vas proximal to the epididymis was present. In the other patients it was absent. The vasa were extremely small and appeared to be about 7.0 to 8.0 cm. long, ending in a small, thickened nubbin about 2 mm. in diameter, situated just within the upper part of the cavity of the scrotum.

DISCUSSION

Embryologically speaking, a disturbance in the normal development of the wolffian duct must be assumed in these cases. The ductus (vas) deferens develops from this organ and connects with the ductuli efferenti (globus major of the epididymis) which are derivatives of the medial group of the mesonephric tubules. Consequently any interference with the evolvement of the mature organ from one part or all of these anlage can produce the various anomalies that have been observed in the vaso-epididymal system.

Although the vaso-epididymal organs and the testes "have a common origin from the mesoderm of the intermediate cell mass" the respective primordia rapidly assume considerable independence of development and the final degrees of function and morphology of these organs may vary greatly.

The cases reported in this series of patients with normal testes and malformation of the vas and in some cases also of the epididymis, exemplify some of the more extreme differences of degree of development that occur between these organs.

It is interesting to note that the quantity of semen in the ejaculated specimen of all these patients with a bilateral absence of the vasa was greatly decreased below that of the normal fertile man. It varied from 0.5 cc to 1.5 cc and averaged 0.92 cc. (This does not include the patient in case 12, who did not bring a specimen, or case 2, from which the quantity of semen was not recorded.) The normally fertile male should ejaculate not less than 2.5 cc, the average being about 3.5 cc.

Hotchkiss has shown, and the experience of others has indicated, that the testis and epididymis produce only about 5 per cent of the semen. Consequently, when this source is cut off, as in the absence of the scrotal portions of both vasa, there still should be about 95 per cent of the normal amount of semen ejaculated. In the cases reported herein only about 15 to 40 per cent of the normal amount of semen was present in the ejaculate. Presumably this would indicate that malformation or disease of some other part or parts of the sexual accessory system, i.e. the prostate, seminal vesicles, etc., was present.

SUMMARY

Twelve cases of abnormal development of the vasa and normal development of the testes are presented.

Operated cases: In only one of these cases was the congenital absence of the vas unilateral. The epididymis on this side was aberrant. The organs on the other side were normal. The diagnosis, based on the physical examination, testicular biopsies and analysis of the semen, was confirmed at operation. In one case a diagnosis of bilateral absence of the vasa in the scrotum, with abnormal epididymides and normal testes, based on the physical examination, testicular biopsies and semen examination, was confirmed at operation. In the remaining case a diagnosis of absence of both vasa in the scrotum with normal epididymides and testes was made from the findings on physical examination, testicular biopsy and semen examination. Operation was permitted on one side only. The preliminary diagnosis on the condition of the organs of this side was confirmed at operation.

Nonoperated cases: The diagnosis in 8 of these 9 cases was made on the findings from the physical examination and analysis of the semen. On the ninth case no semen examination was made. In 3 of the cases biopsy demonstrated normal testicular tissue. In 1 case a mass was felt per rectum apparently involving an internal structure developed from the wolffian body.

Urograms in 1 case showed congenital defect of some of the kidney calyces. In 2 others the urograms were normal.

In the 11 cases with bilateral absence of the vasa and normal testes, the amount of ejaculated semen was greatly decreased from normal. This warranted the assumption that one or more defects of the remaining portion of the sexual accessory system was present.

Congenital anomalies of the vas and epididymis commonly occur in men with impaired fertility.

490 Post St., San Francisco 2, Calif.

REFERENCES

ANSPRENGER, A.: München. med. Wchnschr., **31**: 1707, 1913.
BRACK: Ztschr. f. Urol., **15**: 389, 1921.
GUIZZETTI, P.: Centralbl. f. allg. Path. u. path. Anat., **16**: 387, 1905.
HOTCHKISS, R. S.: Fertility in Men. Philadelphia: J. B. Lippincott Co., 1944.
——: New York, N. Y.: Personal communication.
JORDAN, H. E. AND KINDRED, J. E.: Textbook of Embryology. New York: Appleton-Century, Inc., 1942, 4th ed.
MATHÉ, C. P. AND DUNN, G.: J. Urol., **59**: 461, 1948.
PRIESEL, A.: Virchows Arch. f. path. Anat., **249**: 246, 1924.
——: Handb. d. spez. path. Anat. u. Histol., Henke-Lubarsch, **6** (part 3): 41, 1931.
SIMMONS, F. A., Boston, Mass.: Personal communication.
VEROCAY, J.: Prag. med. Wochnschr., **40**: 113, 1915.
WANGENSTEEN, O. H.: Arch. Surg., **14**: 663, 1927.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

VAS DEFERENS ANASTOMOSIS: A REPORT OF FOUR CONSECUTIVE SUCCESSFUL CASES[1]

BEN D. MASSEY AND EARL F. NATION

Satisfactory repair of the previously sectioned vas deferens is not a hopeless situation, contrary to the common impression. This impression is typified by the following quotation from a statement which recently appeared in the *Journal of the American Medical Association*, in reply to a query on the subject: "Success in repairing a vas deferens cannot be obtained after a properly performed operation for sterility in which a liberal section of vas is excised." This impression is further borne out by the disclosure in O'Conor's recent, excellent article on the subject that over 80 per cent of urologists responding to his questionnaire had never attempted the operation.

The paucity of successful case reports and of literature on the subject, prior to O'Conor's recent paper, confirm this impression. The fact that no standard technique has been developed and that different methods have been used in most of the successful cases reported contribute to the unfavorable view toward vas deferens anastomosis.

Four successive patients in whom bilateral vas deferens anastomosis was performed, utilizing a more or less uniform technique, and in whom viable spermatozoa appeared shortly thereafter, indicate that suitable patients should not be discouraged from having the operation performed. The indications may be the desire for more children, psychogenic impotence resulting from vasectomy, or accidental severance of the vas deferens in the course of other surgery.

LITERATURE

Martin early developed a satisfactory technique for vaso-epididymal anastomosis which has been modified by Hagner and more recently by Michelson, utilizing, at first silver, and recently, stainless steel wire to produce a fistula. The first vasectomy for sterilization in this country was reported in 1899 by Sharp. However, the reports of vas deferens anastomosis in this country have only appeared during the past decade, and these authors have not utilized the wire technique reported in 1901 by Martin.

Strode, in 1937, reported unilateral vas deferens anastomosis on 2 patients, a second operation being necessary in 1 case. Each patient had had vasectomy performed 7 years previously. He utilized plain catgut as a lumen suture and did not remove it, according to the technique of Spath.

Twyman and Nelson, in 1938, reported the successful repair of the vas deferens in a patient who had had a vasectomy 4 years previously. They also used a catgut "hammock" suture for the lumen.

Freiberg and Lepsky, in 1939, reported the successful unilateral restoration of the continuity of the vas deferens 8 years after bilateral vasectomy. They performed a side-to-side anastomosis, using silkworm gut in the lumen.

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, B. C., April 21, 1948.

Nelsen, in 1941, reported an instance of successful bilateral anastomosis of the vas deferens, using a dermal lumen suture and removing it on the seventh day. In the same year, Barker reported an instance of successful bilateral vas deferens anastomosis 4 years after vasectomy, utilizing a plain catgut lumen suture.

In 1945, Cameron performed vas deferens anastomosis successfully, utilizing stainless steel tubes made from 21 gauge intravenous needles, which were left in the vas deferens at the site of anastomosis.

This constituted all of the literature on the subject, except for animal experimental work, done mostly in Europe, until the recent report of O'Conor. He reported having done reunion on 14 men since 1920, with 9 successful results. His questionnaire revealed that 135 urologists had performed the operation 420 times, the outcome being successful in 160 instances.

TECHNIQUE

The surgical technique employed in the cases to be reported here embodied no new principles. However, certain features which will be emphasized seem to contribute to the ease and success of the procedure.

The area of previous vas deferens section is localized and held firmly while a small incision is made in the overlying scrotum. Only the portion of spermatic cord containing the area of section is delivered from the wound. The fibrous tissue intervening between and surrounding the sectioned ends of the vas deferens is carefully dissected off until each end of the vas deferens is exposed. However, the duct is not freed from its sheath. Each end of the tube is then cut across squarely with a razor blade, the cuts extending far enough back to insure patency of each end. The ends, with intervening scar tissue, are then excised. The patency may be tested with a fine probe, dermal catgut, or a blunt straight needle. All bleeding is well controlled to prevent hematoma formation.

Tantalum wire, No. 40 (two cases), or stainless steel wire, No. 32 (two cases), is then threaded on a small, blunt, straight needle which is passed up the vas deferens for a distance of 1 to 3 cm., where it is brought out through the side of the tube. The distal end of the wire is then passed down and out through the distal segment of vas deferens. Tension on the two ends of the wire then brings the ends of the vas deferens together easily and splints them. These are approximated with 3 or 4 interrupted sutures of 00000 chromic catgut, No. 100 cotton, or fine wire, placed in the sheath of the vas deferens. The sheath has been shown by Rolnick's experimental work on dogs to play an important part in re-establishment of the patency of the vas deferens after experimental section and ligation. The ends of the splinting wire are then brought out through the scrotum beyond the respective ends of the incision and the latter is closed. The wires are removed after 8 to 10 days. In each of the cases to be reported, the procedure was performed bilaterally.

CASE REPORTS

Case 1. E. S. (St. Luke Hospital No. H-3274), aged 38, had a vasectomy performed for sterilization in 1942. Four years later another child was desired and vas deferens anastomosis was requested. This was performed on October 10, 1946, using tantalum wire for lumen splint and cotton for sutures. The wires were removed on the ninth postoperative day.

One month following the anastomosis a semen specimen contained an average of ten spermatozoa per high power field, most of them nonmotile.

Four months after surgery a semen specimen contained fifty million spermatozoa per cubic centimeter, 5 per cent being nonmotile and 5 per cent abnormal morphologically.

One year following surgery a semen analysis was as follows: volume 3 cc; sperm count 176,000,000 per cc; 30 per cent nonmotile; 8 per cent abnormal forms.

Case 2. Mr. R. G. (St. Luke Hospital No. 2988), aged 31, had a vasectomy for sterilization in 1941. He had a varicocele on the left side, resulting in partial atrophy of the left testicle.

On April 30, 1947, left varicocelectomy and bilateral vas deferens anastomosis were performed. On the right side the vasectomy had been performed very close to the vaso-epididymal junction. As a result, it was impossible to pass the tantalum wire the usual distance down the distal end of the vas deferens.

The tantalum wires were removed on the tenth postoperative day.

Six months following surgery a semen specimen contained only an occasional spermatozoon. Two months later there still were only 4 or 5 spermatozoa per low power field.

If a further period of observation does not disclose more improvement, a vaso-epididymal anastomosis on the right side might produce a better fistula. The degree of spermatogenesis remaining in the atrophic left testis is dubious.

Case 3. J. T. (St. Luke Hospital No. K-3287), aged 30, had a vasectomy performed in 1941. In March 1947, a semen specimen disclosed no spermatozoa or fragments. On August 29, 1947, the vasa deferentia were anastomosed, using stainless steel wire and 00000 chromic catgut. The splinting wires were removed on the eleventh postoperative day.

Two months following surgery the seminal fluid contained 5,000,000 spermatozoa per cubic centimeter, most of which were motile and normal morphologically.

Three months following the anastomosis the count was 10,000,000 spermatozoa per cubic centimeters, with 25 per cent abnormal morphologically and 30 per cent nonmotile.

Four and one-half months after surgery the count was 50,000,000 spermatozoa per cubic centimeters 50 per cent being nonmotile, and 10 per cent abnormal. His wife at this time thought that she was about 6 weeks pregnant.

Case 4. P. F. (St. Luke Hospital No. K-3453), aged 32, had a vasectomy in 1941. Several centimeters of each vas deferens had been excised. This made the anastomosis somewhat more difficult. However, with stainless steel wire, it was possible to anastomose the ends of the vasa deferentia without tension.

This was performed on September 12, 1947. The splinting wires were removed on the tenth postoperative day.

Two months following anastomosis a semen specimen contained an average of approximately 50 spermatozoa per high power field, most being normally motile and only an occasional one being abnormal morphologically.

Three and one-half months following surgery a semen analysis was as follows: volume 2 cc; count 158,000,000 per cc; 40 per cent nonmotile; 12 per cent abnormal forms.

DISCUSSION

The criteria of success in anastomosis of the vas deferens may vary according to the indications for performing the procedure. Pregnancy should naturally be the final criterion of success when the operation is performed to relieve sterility. However, until better means of determining semen effectiveness are discovered one will have to strive for specimens with characteristics falling within the range of the average "normal" seminal fluid. Of course, many of these patients might not have had "normal" seminal fluid prior to vasectomy and would have had diminishing effectiveness with the passing years. Most patients requesting this procedure are in the fourth decade of life, and in our experience, have not been unusually prolific prior to vasectomy.

Whether or not an entirely normal specimen is produced or pregnancy ensues following vas deferens anastomosis many psychological problems may be solved by the procedure.

It is known that the sperm count may continue to improve for at least a year after anastomosis is performed. So those patients reported here who still have deficient specimens may be expected to continue to improve.

At least, it has been shown that the technique described permits satisfactory anastomosis in most cases. Whether or not performance of the procedure can be shown to be justified by ensuing pregnancy in a sufficiently large percentage of cases can be determined only by the performance of more such operations. It is hoped that the report of these cases will stimulate such work.

SUMMARY

Four cases of vas deferens anastomosis, in which satisfactory canalization was attested by the presence of viable spermatozoa in the seminal fluid, are reported and the technique described.

The impression of hopelessness of vas deferens anastomosis is decried. It is urged that more such operations be performed in order that the prognosis, from the standpoint of subsequent fecundity, may be determined.

112 N. Madison Ave., Pasadena 1, Calif.

REFERENCES

BARKER, J. F.: Anastomosis of the vas deferens. West Virginia M. J., 37: 222, 1941.

CAMERON, C. S.: Anastomosis of the vas deferens. Restoration of fertility five years after bilateral vasectomy. J. A. M. A., 127: 1119, 1945.

FREIBERG, H. B. AND LEPSKY, H. O.: Restoration of the continuity of the vas deferens eight years after bilateral vasectomy. J. Urol., 41: 934, 1939.

HAGNER, F. J.: J. A. M. A., 107: 1851, 1936.
MARTIN, E.: Uni
MICHELSON, L.: permanent fistula with use of stainless s 46.
NELSEN, M. T.: Obst., and Gynec., 49: 152, 1941.
O'CONOR, V. J.: Anastomosis of vas deferens after purposeful division for sterility. J. A. M. A., 136: 162, 1948.
ROLNICK: Quoted by Strode.
SHARP, H. C.: New York Med. J., 75: 411, 1902.
SHARP, H. C.: J. A. M. A., 53: 1897, 1902.
STRODE, J. E.: A technique of vasectomy for sterilization. J. Urol., 37: 733, 1937.
SPATH, F.: On the question of operation for restoration of permeability of the spermatic ntralbl. f. Chir., 61: 454, 1934.
—: . operations for sterilization in animal experiment and in 48: 36, 1935.
TW . S.: Vas deferens anastomosis. Urol. and Cut. Rev., 42: 586, 1938.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

MALIGNANCY IN CRYPTORCHIDISM[1]

WILLIAM A. CARROLL

The incidence or frequency of malignancy in cryptorchidism is reported perennially with an amazing variance in the conclusions arrived at by the essayists. Many writers state there is little or no incidence; on the other hand, it is claimed that when the incidence of undescended testicles is compared to the incidence of malignant cryptorchidism, this correlation is from 20 to over 50 times higher than could be expected by chance association. Malignant cryptorchidism is asserted to represent from 9 to 15 per cent of all the malignant tumors of the testicle.

In the face of this high statistical frequency, and never having seen a malignant undescended testicle, I wondered why these figures do not coincide with the general experience of urologists. In urology many other congenital anomalies *exist; viz., double kidneys, ectopic (pelvic) kidneys or horseshoe kidneys, but we* do not hear similar claims of a high malignancy incidence. Perhaps the conviction of LeComte, when he stated in 1851 that undescended testicles frequently became malignant, still lingers with us and refuses to be extirpated from the literature.

Most authors due to their own paucity of cases and experience (and this includes most of the urological text books) refer to the conclusions of their predecessors for support. The literature is littered with misquotations and distortions of the words of the original authors (Campbell) and these complicate the picture when these misquotations are used in drawing up statistics.

The early writers assumed that because the congenital anomaly of undescended testicle resulted in maldevelopment or lack of development, that this made malignant changes more likely than in the fully developed and descended scrotal testicle. In recent years, the increasing number of malignancies after orchidopexy (Chevassu, Cabot, and Gilbert) and the reports of testicular malignancies in fully descended testes in the presence of a benign cryptorchid on the contralateral side cast a reasonable doubt on the original contention. At the present time, those favoring high incidence (Cabot, Campbell, Gilbert and Hamilton and Hinman) state that cryptorchidism is not necessarily the cause of the malignant changes because of the ectopic residence or maldevelopment but, that the statistics in the literature definitely show a high ratio of incidence between malignant cryptorchidism and undescended testicles taken as a whole.

For the purposes of this discussion, cryptorchidism is defined as maldescent or nondescent of the testicle under three sub-divisions:

a) abdominal proximal to the internal inguinal ring; b) inguinal residing in the inguinal canal; c) extrascrotal locations—pubic, femoral, penile or perineal.

Let us examine these statistics showing such a high incidence of malignancy in cryptorchids when compared to the incidence of undescended testicles in general and determine their accuracy and reliability. The pattern of assembling data for these statistical tables follows one of two types of procedure:

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, B. C., April 20, 1948.

1) Individual series with a small number of malignancies.
2) Compilation of reported series supplemented with estimated or hypothesized figures from reliable sources for the missing data required for statistical purposes.

Four groups of figures are necessary for either of these two approaches to statistical tables:

1) Total male hospital admissions or estimated total male population.
2) Total or estimated total number of testicular malignancies.
3) Total number of malignancies in undescended testicles.
4) Total or estimated total number of undescended testicles.

Consider now separately each of the four prerequisites to the statistical tables:

TOTAL MALE HOSPITAL ADMISSIONS OR ESTIMATED TOTAL MALE POPULATION

Male hospital admissions are usually readily obtainable if the record room segregates male and female entries for the period of years under study. One common source of error develops if the hospital gives a new hospital number for each re-admission or if outpatients are listed. There is usually no separation into age groups, and new born infants, children, and those under 20 years of age (where malignancy is rare) swell the total and distort the percentage tables. Estimated total male population figures are available every 10 years from the U. S. Census Bureau and can be considered accurate, but the same criticism can be levied against them as against hospital records for all ages of male patients are included (whereas 86 per cent of testicular malignancies occur between ages of 20 and 50), and all cases listed as dying from a testicular tumor do not have pathological confirmation.

TOTAL OR ESTIMATED TOTAL NUMBER OF TESTICULAR MALIGNANCIES

The total number of malignant testicles in a hospital series should be assembled with ease if care is taken to exclude all cases not pathologically certified. Hospital statistics often index wrongly clinical diagnoses that later prove to be hydroceles, gummata, tuberculosis or metastatic lesions from organs other than the testis. One is impressed on seeing the figures that testicular malignancy is a rare tumor (about 0.05 per cent in male patients as a whole and about 0.58 per cent of all malignant tumors—U. S. Census Bureau). Hence no individual or hospital or clinic is ever going to accumulate a series of numerous cases. The rarity of this neoplasm is shown again (Gilbert and Hamilton) by U. S. Census Bureau records of only 270 deaths a year in the United States.

TOTAL NUMBER OF MALIGNANCIES IN UNDESCENDED TESTICLES

This subdivision of testicular malignancies is extremely small numerically in any given hospital series and for some reason they are listed apart from testicular neoplasms as a whole (possibly from the original concept of their potential malignancy because of their ectopic position). The published incidence of malignant cryptorchidism in relation to testicular malignancies as a whole varies from 8 to 15 per cent, i.e., Campbell 8 per cent, MacKenzie and Ratner 8 per cent, Gilbert and Hamilton 9 per cent, Rubaschow 11 per cent, Hinman 12.2 per cent, Dean 13 per cent, Chevassu 13.7 per cent and again 11 per cent, and Scott 15 per cent. In opposition to these figures Cunningham reports 1 in 67 cases, Eccles none in 854 cases, Kocher 1 in 1000 cases and Coley none in 1357 cases.

TOTAL OR ESTIMATED NUMBER OF UNDESCENDED TESTICLES

Figures on the incidence of undescended testicles are most confusing and uncertain. The hospital recorded cases are ridiculously few. The hospital diagnosis sheet gives pathological rather than anatomical diagnoses, and the number of cases reported represent those with some complaint or treatment referable to the undescended testis as the cause for admission. The tonsil, appendix, fracture, pneumonia or cardiac case with an undescended testicle found on routine physical examination seldom, if ever, has the cryptorchid recorded on the diagnosis sheet. The record room is asked to supply anatomical diagnostic figures whereas it is possible for them to report only the pathological diagnoses listed on patients' histories by the house staff. This low incidence of undescended testicles in the hospital records has a very vital bearing on the problem as it is the essential figure necessary in the statistical proof that malignancy is proportionally higher in cryptorchidism than in the fully descended testis.

Nondescent of the testis occurs in 14 per cent of boys under 1 year of age and this drops to 4 per cent between the first and fifth year of life (Lowsley and Kirwin) very few cryptorchids descend spontaneously after the fifth year. This age variation makes the proper handling of figures on incidence bewildering, even if they are accurate. Should the incidence of cryptorchidism in all infants and boys be included with the adult males since they were included in hospital admission and total population totals?

The uncertainty as to the true incidence of cryptorchidism deepens when the published statistics are enumerated, i.e., Marshall 0.1 per cent, Hempel 0.2 per cent, Gilbert and Hamilton 0.23 per cent, World War I records 0.31 per cent, Howard 0.6 per cent, Baumrucker 0.75 per cent and Coley 4.7 per cent; a variation from 1 in a 1,000 to 75 in a 1,000. Both extremes are out of line but still it would appear that there are a large number of adult male patients with cryptorchidism and hence all of us occasionally should see cases of malignancy in this group.

Table 1 will clarify the two methods of approach to these statistical studies of malignancy in cryptorchidism.

In the University of California Hospital chart (table 1), the first line of figures were published by Hinman and Benteen in 1936, showing 39,359 male hospital admissions including 40 malignant testicles, 3 abdominal malignant testicles, and a total of 155 undescended testicles. The second line was added by me to their totals bringing the series up to date (1913–1948 or 35 years). Thus there were approximately 65,072 male admissions in 35 years, a figure that is approximate as male and female hospital admissions have not been segregated for the past 4 years and as each patient received a new hospital number regardless of the number of re-admissions up to 1944.

Seventy-four proven cases of malignant testicles were found and, of these, 3 were abdominal and 1 inguinal in type, a ratio of 1 malignant case to each 880 hospital entries.

Only three hundred and seventy-four undescended testicles were recorded most of which were in boys. Of the recorded undescended testicles 178 were in patients on whom an orchidopexy was performed; hence, since these figures are incomplete, the statement that there was one malignant cryptorchid to each 94 undescended testicles is inaccurate.

In the Peter Bent Brigham Hospital (table 1) the 27 year total (1913–1939) of approximately 50,000 male hospital admissions showed 19 malignant testicles, a ratio of 1 malignant case to each 2630 hospital entries. One abdominal and 1 inguinal malignant cryptorchid was found and a total of 182 undescended testicles, a ratio of 1 malignant cryptorchid to each 91 undescended testicles. From my experience with the University of California Hospital records, it seems doubtful that this total for the undescended testicles reported for Peter Bent Brigham Hospital (7 cases a year for 27 years) is correct, and constitutes all the undescended testicles passing through that hospital from 1913 to 1939. All that can be accepted from these charts is that testicular malignancy is rare and malignant cryptorchidism is extremely rare. The use of an inaccurate premise makes untenable the claim for a higher incidence of malignancy statistically in the undescended as compared to the normally descended testes.

TABLE 1. *University of California Hospital Statistics*

PERIOD	MALE ADMISSIONS ALL AGES)	TOTAL MALIGNANT TESTICLES	TOTAL MALIGNANT UNDESCENDED TESTICLES	TOTAL TESTICLES UNDESCENDED
1913–June 1935	39,359	40	3 Abdominal	155
June 1935–Jan. 1948	(*) 25,713	34	1 Inguinal	219
35 Years—Totals	(*) 65,072	74	4	374
(*) Approximate Total	1 in 880		1 in 94	
Peter Bent Brigham Hospital Statistics				
1913–1939				
27 Years—Totals	(*) 50,000	19	2 {1 Abdominal 1 Inguinal}	182
(*) Approximate Total	1 in 2630		1 in 91	

Gilbert and Hamilton secured data from the U. S. Census Bureau showing that the 1930 male population in the United States was 62,137,080 and also that the annual reported deaths from testicular tumors was 270; arbitrarily assuming the average testicular tumor patient lived 3 years, the annual death rate would be 810 incidence of 0.0013 per cent (table 2). From statistics gathered in the United States and Europe on 9,744,097 men examined for the military service, an incidence of 22,665 undescended testicle cases was found varying in percentage from 0.102 to 0.5 with a mean average of 0.23 per cent incidence (Marshall, Rennes, Myrdacz, Love and Davenport and Southam and Cooper).

Having estimated the annual death rate from testicular tumors and the overall incidence of undescended testicles, they proceed to apply it to a compiled series of approximately 7,000 malignant testicular tumors 840 of which were in undescended testicles 1 in 11 or 9 per cent. When the estimated incidence of undescended testicles (0.23 per cent) is applied to this ratio (11 divided by 0.23), the incidence of malignancy in cryptorchidism is claimed to be 48 times greater than in the normally descended testicle.

TABLE 2. *Gilbert and Hamilton Statistics*

TOTAL 1930 U.S. MALE POPULATION	ESTIMATED MALIGNANT TESTICLES	TOTAL MALIGNANT UNDESCENDED TESTICLES IN SERIES	ESTIMATED UNDESCENDED TESTICLES
	270 Reported Deaths ×3 Years Average After Life		
62,137,080	810 Tumors		
Incidence	.0013%		
	Total Malignant Testicles in Series 7000	840	22,665 in 9,744,097 Me. or .23%
	9% or 1 in 11		
		Incidence $\frac{11}{.23}$ = 48 Times	

H. E. Campbell Statistics

TOTAL MALE HOSPITAL ADMISSIONS	TOTAL MALIGNANT TESTICLES	TOTAL MALIGNANT UNDESCENDED TESTICLES	ESTIMATED UNDESCENDED TESTICLES
505,000	394	31	.23%
Incidence .078	8% or 1 in 12.7		
		Incidence $\frac{12.7}{.23}$ = 55 Times	

In the H. E. Campbell statistics, a compiled series is given showing 505,000 male hospital admissions with a total of 394 malignant testicles—incidence 0.078 per cent. Of 394 malignancies, 31 were in undescended testicles or a frequency of 1 in 12.7 (8 per cent). Accepting Gilbert and Hamilton figures for the estimated incidence of undescended testicles (0.23 per cent), Campbell's frequency of malignancy in cryptorchidism is shown as 55 times greater (12.7 divided by 0.23) than in the normally descended testicle.

In criticism of the statistics of Gilbert and Hamilton and of Campbell, we find that the reported annual death rate from testicular malignancies was 270 (U. S. Census Bureau). This was considered too low and each testicular tumor case was allowed to live 3 years, raising the yearly incidence to 810. Contrarily the reported figures showing a relatively high frequency of undescended testicles were ignored and a mean average of 0.23 per cent was obtained by accepting data having from a 0.102 per cent to 0.5 per cent incidence. As a result, the statistics naturally demonstrate a high incidence of malignant cryptorchidism with the authors' hand pick and hypothesize figures favoring their viewpoints.

The conclusions drawn from these statistics are not acceptable because of the flaws pointed out and a reasonable doubt as to their reliability, particularly when high incidence does not coincide with medical experience. The statistical frequency of malignant cryptorchidism will never be amenable to mathematical study until generally accepted accurate data are presented and proven. All past statistical studies on this subject therefore should be disregarded as being definitely open to question.

TABLE 3 *Have you personally ever seen or treated a malignant intra-abdominal or a malignant imperfectly undescended testicle?*

American Urological Association		
Yes	159	24%
No	503	76%
Total	662	
Western Section, American Urological Association		
Yes	33	19%
No	141	81%
Total	174	

Dissatisfied with the available statistics and convinced the subject did not lend itself to acceptable statistical review, I found myself with the problem unanswered. Never having seen a malignant cryptorchid, I wondered what the personal experience of other urologists was on malignancy in cryptorchidism. With this in mind a questionnaire was mailed to each of the active and associate members of the Western Section of the American Urological Association and to each member of the American Urological Association.

A total of 662 replies were received, including numerous personal communications and reprints expressing the various men's ideas and opinions. Perusal of the cards and letters showed the vast majority of urologists had never seen a malignant cryptorchid and while doubting the high incidence reported in the literature, they could not refute the claims from their own personal experience. Approximately 15 per cent of the urologists expressed positive convictions, either for or against high frequency. In analyzing the information obtained from the questionnaire all the replies listed under the American Urological Association and the responses of the Western Section of the American Urological Association were separated for special tabulation. Seventy six per cent of the A.U.A. members and 81 per cent of the Western Section A.U.A. members have never seen a malignant undescended testicle. See table 3.

One hundred and twenty six A.U.A. members and 33 Western Section A.U.A. members report a sum total of 285 malignant cryptorchids seen by them. It is possible that some of these cases are reported by more than one man but it was the trend, rather than statistical facts that was desired. Two A.U.A. members reported the highest personal series of 7 each and no other member of either the A.U.A. or the Western Section reported more than 4 cases each. Several men wrote of seeing increasing numbers of malignant testes following orchidopexy, particularly in the Army and Navy hospitals during World War II. See table 4.

Regarding the question as to whether cryptorchidism tends to produce testicular atrophy or malignancy, an avalanche of comment, besides the response to the query, resulted.

TABLE 4. *What was the number and location of each of the malignant types?*

	ABDOMINAL	INGUINAL	OTHER EXTRASCROTAL LOCATIONS	TOTALS
126 A. U. A. members	115	97	8	220
33 Western Section members	31	32	2	65
Totals	146	129	10	285

Dr. Lloyd G. Lewis reported *12* cases from a series of 250 *malignant testicles* at Walter Reed Hospital.

Two A. U. A. *members reported* series of *7* cases each.

No other member of either the A. U. A. or the Western Section A. U. A. reported more than a total of *4* cases.

The word "atrophy" was used on the card because of a necessary economy in words, but its misuse was pointed out repeatedly by the respondents. Atrophy would presuppose an originally normal organ; so maldevelopment or lack of development of the spermatogenic elements with a relative increase in the interstitial cells due to the cryptorchid position was the consensus of opinion expressed and that true atrophy with loss of all cell elements occurred only after puberty or possibly only as late as 20 years of age atrophy following orchidopexy was a common comment. The necessity for orchidopexy into the scrotum between the ages of 8 and 12 was emphasized to avoid trauma, hernia and atrophy and to permit the development of spermatogenesis, if possible, recognizing the surgical hazards of possible necrosis, atrophy or later malignancy. Testicular malignancy after orchidopexy was conjectured as being due to the surgical manipulation, hormonal over-stimulation of a testis attempting, after liberation, to obtain the status of a normal organ. It was the consensus of opinion that malignancy after orchidopexy would have developed regardless of whether the gland was in the scrotum or in its previous cryptorchid position.

Accepting maldevelopment or lack of development of the spermatogenic elements of the anatomically misplaced testicle as the definition of the term "atrophy", the majority favored this finding, with eventual loss of all cellular elements without orchidopexy. However over half of the questionnaires list malignancy as "possible", indicating that those who replied were influenced by the literature and their own lack of experience.

CONCLUSIONS

This summation of the replies on the personal experience with malignant cryptorchidism from 662 urologists is not presented as a statistical study. It is offered only as a definite refutation by the urologists responding of the validity of the claims in the present literature that there is a proven higher statistical incidence of malignant change in the undescended testicle than in the normally descended testicle. Each of you may form your own opinion from available data, but, my own uncertainty on this subject has been remedied by this consultation with my confreres in urology and I feel justified in drawing the following conclusions:

Malignant testicular tumors are rare.

Malignancy in cryptorchidism is still more rare and should be classified on its anatomical location as a form or sub-division of testicular malignancy in general and not as a separate entity.

The present statistics proving the higher incidence of malignancy in cryptorchidism cannot be accepted because there is a reasonable and justifiable doubt as to the accuracy of the factual premises upon which they are based.

Any urologist will be fortunate to see or treat a single case of malignant cryptorchidism *in his life span of practice.*

The incidence of malignancy in cryptorchidism from the actual cases reported is so minute that the potentiality of its malignancy cannot be used as an indication for either orchidopexy or orchidectomy.

450 Sutter St., San Francisco 8, Calif.

REFERENCES

Auerbach, O., Brines, O. A. and Yaguda, A.: Neoplasms of the testis. J. Urol., 56: 368–374, 1946.

Bagg, H. J.: Experimental production of teratoma testes in fowls. Am. J. Cancer, 26: 69–84, 1936.

Baumrucker, G. O.: Incidence of testicular pathology. Bull. of U. S. Army Med. Dept., 5: 312–314, 1946.

Bulkley, K.: Malignant disease of the testicle retained within the abdominal cavity. Surg., Gynec. & Obst., 17: 703–719, 1913.

Burdick, C. G. and Coley, B. L.: Abnormal descent of the testicle. Ann. Surg., 84: 867–878, 1926.

Bryant, T.: Cases of malposition of the testicle. Guy's Hosp. Rep., 13: 419–430, 1867.

Cabot, H. and Berkson, J.: Neoplasms of testis. New Eng. J. Med., 220: 192–195, 1939.

Campbell, H. E.: Incidence of malignant growth of the undescended testicle. Arch. Surg., 44: 353–369, 1942.

Chevassu, M. and Ramond, C.: Tumeurs du testicule. Thesis of Paris, 1906; Presse méd., 18: 363, 1910. Cancers testiculaires developpés sur les testicules ectopiques après leur abaissement operatoire. J. d'urol., 47: 59–70, 1929.

Christoffersen, W. F. and Owen, S. E.: Neoplasms in cryptorchids. Am. J. Cancer, 26: 259–268, 1936.

Coley, W. B.: Results of one thousand operations [illegible] oral hernia performed between 1891 and 1902. [illegible]

——: The treatment of the undescended or maldes[illegible] hernia. Ann. Surg., 48: 321–350, 1908.

——: *Cancer of the testis. Ann. Surg., 62: 40–73, 1915.*

——: The treatment of the undescended or maldescended testis with particular reference to end results. South. Surg. Tr., 31: 79–101, 1919.

COOPER, E. R. A.: Histology of retained human testes at different ages. J. Anat., **64:** 5–27, 1929.
COUNSELLER, V. S.: Cryptorchidism: Treatment and results in one hundred cases, J. Urol., **30:** 327–343, 1933.
CUNNINGHAM, J. H.: New growths developing in undescended testicles. J. Urol., **5:** 471–479, 1921.
DEAN, A. L., JR.: Treatment of teratoid tumors of the testis with radium and x-ray. J. Urol., **13:** 149–165, 1925.
——: Treatment of teratoid tumors of the testis with radium and the roentgen ray. J. Urol., **21:** 83–101, 1929.
——: Teratoma testis with metastases controlled by irradiation. Am. J. Surg., **7:** 276–280, 1929.
——: Teratoid tumors of the testis. J. A. M. A., **105:** 1965–1972, 1935.
ECCLES, W. M.: The anatomy, physiology and pathology of the imperfectly descended testis. Lancet, **1:** 569–576, 1902.
FRIEDMAN, N. B. AND MOORE, R. A.: Tumors of testis. Military Surg., **99:** 573–593, 1946.
GILBERT, J. B.: Development of testicular tumors after orchidopexy. J. Urol., **46:** 740, 1941.
—— AND HAMILTON, J. B.: Incidence and nature of tumors in ectopic testes. Surg., Gynec. & Obst., **71:** 731–743, 1940.
—— AND MOODY, H. C.: Diagnosis and treatment of malignant testis tumors. Urol. & Cutan. Rev., **44:** 89–94, 1940.
HAGNER, F. R.: In Nelson's Loose-Leaf Living Surgery. New York: Thomas Nelson and Sons 1928, vol. 6, chap. 2, p. 153.
HAMILTON, J. B. AND GILBERT, J. B.: Bilateral testicular cancer, incidence, nature and bearing upon management of the patient with a single testicular cancer. Cancer Research, **2:** 125–129, 1942.
HIGGINS, C. C.: Malignant tumors of the testicle. Ann. Surg., **87:** 263–291, 1928.
—— AND BUCHERT, W. I.: Malignant tumors of the testicle. Am. J. Surg., **43:** 675–687, 1939.
HINMAN, F.: Tumors of the testis. In Cabot, H., Modern Urology, Lea & Febiger, Philadelphia: ed. 2, vol. 1, 1924, pp. 580–609. Also ed. 3, vol. 1, 1936, pp. 562–602.
——: Principles and practice of urology. Philadelphia & London: W. B. Saunders Co., 1935, pp. 430–439.
—— AND BENTEEN, F. H.: Relationship of cryptorchidism to tumor of the testis. J. Urol., **35:** 378–381, 1936.
KEYES, E. L.: Urology. New York and London: D. Appleton & Co., 1924, pp. 525–529.
LOVE, A. G. AND DAVENPORT, C. B.: Defects found in drafted men: Statistical information compiled from the draft records. Washington, D. C.: Government Printing Office, p. 164, 1920.
LOWRY, E. C., BEARD, D. E., HEWIT, L. W. AND BARNER, J. L.: Tumor of the testicle; analysis of 100 cases. J. Urol., **55:** 373–384, 1946.
LOWSLEY, O. S. AND KIRWIN, T. J.: Clinical Uurology. Baltimore: Williams & Wilkins, 1944, ed. 2, vol. 1, pp. 451–462.
LUND, F. G.: New growths in undescended testes. Boston M. & S. Jour., **190:** 533–536, 1924.
MACKENZIE, D. W. AND RATNER, M.: Tumors of the testis. Surg., Gynec. & Obst., **52:** 336–349, 1931.
—— AND RATNER, M.: Malignant growths in undescended testes. J. Urol., **32:** 359–369, 1934.
MURRAY, O. B. AND EWERT, E. E.: Malignant disease in undescended testes. Surg. Clinics of No. Amer., **27:** 709–712, 1947.
PACE, J. M.: The histologic and pathologic anatomy of the retained testis. Proc. Staff Meet., Mayo Clinic, **10:** 726–730, 1935.
PACK, G. T. AND, LEFEVRE, R. G.: The age and sex distribution and incidence of neoplastic diseases at the Memorial Hospital, New York City. J. Cancer Research, **14:** 167–294, 1930.
REA, C. E.: Malignancy of the testes with special reference to undescended testis. Am. J. Cancer, **15:** 2648–2658, 1931.
SMITH, G. G.: In Practice of Surgery edited by Dean Lewis. Hagerstown, Md.: W. F. Prior Co. Inc., 1928, vol. 9, chap. 27, pp. 13–20.
SOUTHAM, A. H., AND LINELL, A. E.: The pathology of neoplasms of the testis. Brit. J. Surg., **11:** 223–233, 1924.
—— AND COOPER, E. R. A.: Hunterian lecture on the pathology and treatment of the retained testis in childhood. Lancet, **1:** 805–811, 1927.
THIESSEN, N. W. AND WALTERS, W.: Cryptorchidism. Proc. Staff Meet., Mayo Clinic, **10:** 132–139, 1935.
WANGENSTEEN, O. H.: The undescended testis. Arch. Surg. **14:** 663–731, 1927.
——: Undescended testis, its fate after satisfactory scrotal anchorage. Ann. Surg., **102:** 875–904, 1935.
WESSON, M. B.: Tumours of the testicle. Brit. J. Urol., **11:** 338–349, 1939.
YOUNG, H. H. AND DAVIS, D. M.: Young's Practice of Urology. Philadelphia and London: W. B. Saunders Co., 1926, vol. 2, pp. 113–118.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

OSTEITIS OF THE SPINE[1]

CHARLES D. DONAHUE

I believe that osteitis of the spine sometimes occurs as a complication of prostatic surgery, but that the condition is comparatively rare. The Cumulative Index since 1938 lists no publications on the subject. Many infected prostates are operated upon, which could be the source of infection transported from this primary site to some other part of the body. Undoubtedly changes in the bone occurred more frequently than was suspected, especially before the days of the antibiotics and sulfonamides. Frequently references to inflammatory changes in the os pubis and other pelvic bones, secondary to prostatic surgery, cannot be attributed to direct trauma during operation. Silver states that the condition does not always remain limited to the pubic area, but the process may extend through the ischial bones and occasionally even to the acetabula, with serious consequences to one or both hip joints.

The etiology and pathogenesis of osteitis of the spine are not clear, but the distribution of the infection seems to follow the same pattern as that noted in the metastases to the spine from carcinoma of the prostate. Batson has pointed out, or at least inferred, that definite infectious or malignant material may be carried by the blood stream through the vertebral system of vessels. He has pointed out that the dorsal vein of the penis is an integral part of the prostatic venous plexus which drains into the vertebral plexus, providing the pattern that explains the spread of carcinoma of the prostate. Once within the lumen of the vessels the metastatic material can be transmitted to form deposits in the vertebral column, pelvic girdle, or even the skull. Although usually referring to malignant cells, it is not difficult to theorize that infected material can be transported and spread in the same manner. Possibly this is one explanation of the so-called "urethral chill" following instrumentation of the urethra. If the infectious material is transient and does not lodge at some definite point the patient may escape the grave complication of distant infection or abscess of some soft or bony structure. That osteitis of the spine may be a serious complication is borne out by the following 2 cases.

CASE REPORTS

Case 1. W. T. G., a man aged 71, was admitted to the Sacred Heart Hospital on April 12, 1941, because of recurrent hematuria. He had had a transurethral resection at my hands in 1938. Renal and bladder studies prior to this admission had shown that the blood came from the prostatic urethra. Clinically the prostate was benign, and biopsy showed the prostatic tissue to be adenomatous hyperplasia with acute ulcerative prostatitis. The gross hematuria was complicated by subacute attacks of bladder infection, relieved to some extent by sulfanilamide.

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, British Columbia, April 21, 1948.

Physical examination showed a well nourished and well preserved man with temperature 97.6 F., pulse 92, and blood pressure 160/90. The eye grounds showed 2 plus retinal arteriosclerosis, and the thyroid was somewhat enlarged. The heart was normal, except for slight aortic configuration. Electrocardiogram showed slight left axis deviation, with normal conduction time. Hemoglobin was 105 per cent, red count 4.1 million, and white count 9300, with an essentially normal differential count. The serum acid phosphatase was not done. The urine contained a few blood cells, but cultures were not done. Cystoscopy was attempted, but was abandoned on account of profuse bleeding.

On April 12, the same day, a prostate weighing 40.1 gm. was removed easily by a 1-stage suprapubic procedure. The pathologic diagnosis was benign hyperplasia without evidence of malignancy.

Convalescence was uneventful until the thirteenth day when there was severe bleeding from the bladder and the patient was returned to surgery for transurethral aspiration of blood clots. The prostatic fossa was covered with healthy appearing granulation tissue. From this day on there were varied complications, including in succession a pulmonary embolism of moderate extent, thrombophlebitis of the right leg, and bilateral pyelitis. For the next 5½ weeks his temperature curve was quite irregular and at one time reached to 104.4 F. It gradually receded to normal and he was discharged on the fifty-eighth postoperative day, voiding normally and, except for generalized weakness, in apparently good condition.

There were no further complaints regarding the bladder, but there developed a gradual onset of lumbar pain. Sitting or standing caused pain, with the greatest discomfort noted on rising from the lying to the sitting or from the sitting to the standing position.

X-rays of the spine on October 19, 1941, six months after operation, (fig. 1, *A*) revealed cortical and subcortical bony destruction of the inferior aspects of the tenth thoracic vertebra and the adjacent superior cortex of the eleventh thoracic, with narrowing of the intervertebral space (fig. 1, *B*). The lateral view showed the process to be predominantly anterior.

The patient was fitted with a brace extending from the axillae to the hips, and this was worn with great relief from pain. The progress of bony repair was followed with x-rays, with a striking change manifest on August 29, 1944, some 3 years later (fig. 2, *A*). The films then revealed bony bridging laterally with fusion of the tenth and eleventh thoracic vertebral bodies by sclerotic bone. There was no evidence of an interspace shown (fig. 2, *B* and *C*). Films taken 1 year later, November 26, 1945, gave the same findings, showing the lesions to be definitely stable. This patient expired in February 1948, of an acute coronary thrombosis, but no autopsy was obtained.

Case 2. W. E. M., a man, aged 60, was admitted to the Sacred Heart Hospital on February 25, 1946. A prostatic resection had been performed elsewhere some 28 months prior to admission here. Some 13 months after operation gross hematuria had appeared with nocturia some 2 times each night. The hematuria occurred at intervals for a month or two and then ceased. Several months later bleeding and nocturia again appeared, which were treated by dilatations of the urethra After the first dilatation there was a fever to 104 F, followed by a low grade fever for a week After the next treatment he had a severe chill resulting in hospitalization for treatment with penicillin and sulfonamides There had been 2 attacks of fever since that time, and this admission to the hospital was due to another severe chill associated with fever I saw him in consultation with Dr O A Waller

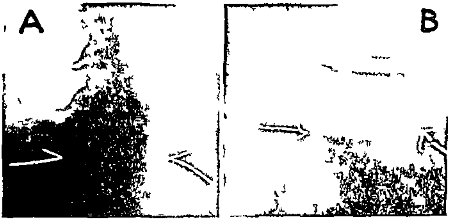


FIG 1 Case 1 *A*, left, October 19 1941 Cortical and subcortical bony destruction of adjoining surfaces of thoracic vertebrae *B* right, lateral view, showing process predominantly anterior

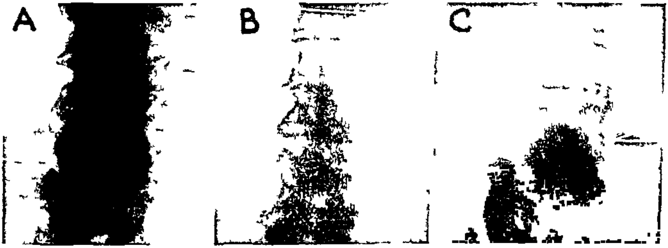


FIG 2 Case 1 *A*, left, August 29, 1944 Bony bridging seen between vertebrae *B*, middle November 26, 1945 Revealing lesions definitely stable *C*, right same date as *B* Lateral view showing bridging and obliterated intervertebral space

Physical examination revealed nothing abnormal The urine showed only a few red cells and pus cells The blood count showed 3 4 million reds and 12,900 white cells The serum acid phosphatase was not determined

The 24 F cystoscope was passed easily through a rather snug posterior urethra The bladder mucosa was normal There was an excellent canal through the prostate, but a small amount of hypertrophied tissue remained near the verumontanum The surface of the prostatic urethra was covered with a network of fine varicosities, and the verumontanum was slightly inflamed Cultures of the urine from the right kidney showed gram negative bacilli of the colon group, while the urine from the left kidney gave only diphtheroids

On March 4, 1946, a week after admission, transurethral prostatic resection was done, $4\frac{1}{2}$ gm tissue being removed from the region of the verumontanum.

The pathological diagnosis was benign hyperplasia of the prostate with no evidence of malignancy.

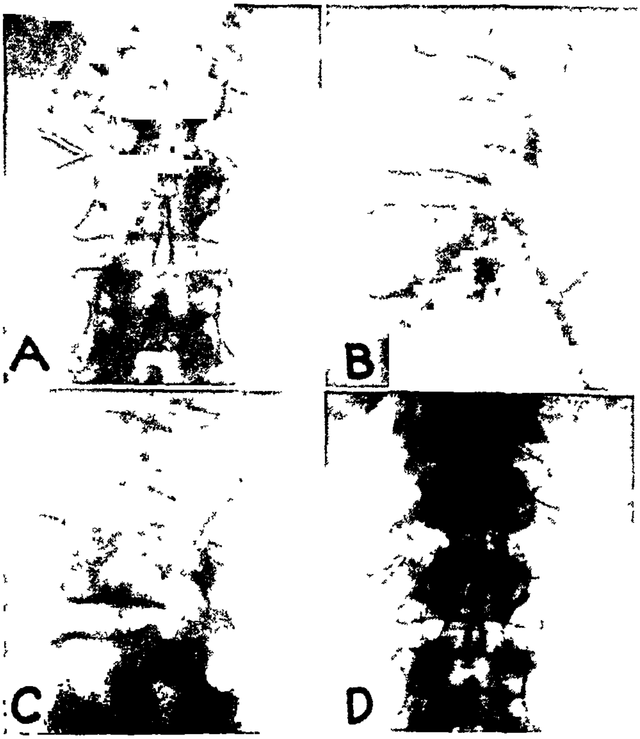


FIG. 3. Case 2. *A*, upper left, March 19, 1946. Showing slight deossification of right superior aspect of third lumbar vertebra. *B*, upper right, lateral view, showing anterior location of destructive process. *C*, lower left, April 4, 1946. Showing dissolution of cortex. *D*, lower right, April 19, 1946. Early evidence of bony bridging between vertebrae has already appeared.

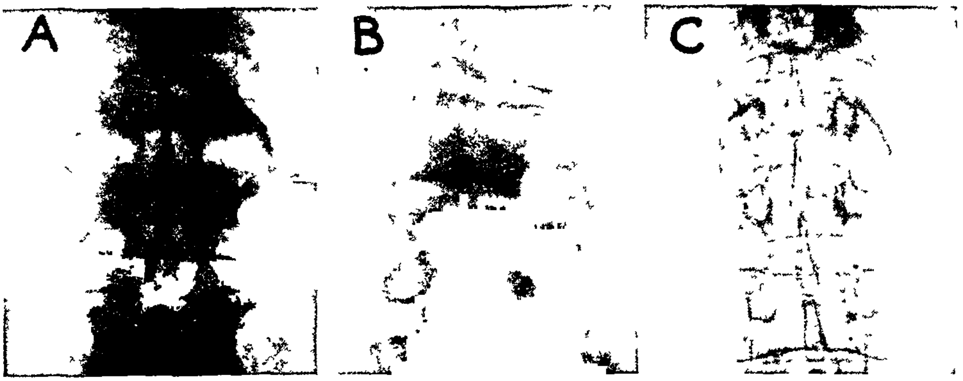


FIG. 4. Case 2. *A*, left, June 19, 1946. Marked increased density of lateral bridging. *B*, middle, lateral view, showing dense bony bridge between vertebrae. *C*, right, January 21, 1948. Well developed bony bridge between vertebrae, with restitution of vertebral diameter and of intervertebral space.

The postoperative course was smooth, and he was discharged on the tenth day. He was readmitted a week later with a temperature of 99.4 F. and complaining of pain in the midlumbar area. The urine was loaded with pus. The red count was 4.9 million and the white count 9100, with 79% segmented neutrophiles. The sedimentation rate was elevated. The heart and chest were normal and the abdomen was soft. He complained of intense pain on standing, stooping, or bending laterally.

X-ray of the spine (fig. 3, *A*) showed slight deossification on the right superior aspect of the third lumbar vertebral body, which the lateral view (fig. 3, *B*) demonstrated to be anterior. The patient was placed in a plaster body cast from the axillae to and including the hips. Two weeks later the x-rays (fig. 3, *C*) showed dissolution of the cortex over the anterior four-fifths of the superior margin of the third lumbar vertebral body. On April 19, 1946, only 2 weeks later, there was evidence of early bony bridging between the second and third lumbar vertebrae (fig. 3, *D*). Films taken 2 months later (June 19, 1946) demonstrated increased density of the lateral bony bridging. (fig. 4, *A* and *B*). Films were taken on January 21, 1948 (fig. 4, *C*) which revealed well developed bony bridging, with restitution of the vertical diameter of the vertebral body, and a normal intervertebral space. The intervertebral space was not shown to be narrowed in any of the series of films on this patient. He has a definite ankylosis of the lumbar spine, but has returned to his work at the dental chair.

SUMMARY

Two cases of osteitis of the spine have been presented, both of which have been followed with repeated x-rays showing the initial osteitis and the subsequent changes. The fixation of the spine by calcification and ossification is contrary to that seen in metastases from carcinoma of the prostate. Study of the literature leads one to believe that these lesions as well as osteitis of the pubis may be blood borne. Instrumentation or surgery of the bladder neck can distribute infectious material into the small venules which are tributary to a general plexus leading to the vertebral plexus. The x-ray is an invaluable aid in diagnosis. The changes in the cortex and in the subcortical bone, followed by bone destruction and finally by re-establishment of the bony architecture, with fixation of the articular surfaces, can be well shown.

Grateful acknowledgement is made to Dr. John R. Seeley for his careful interpretation of the roentgenograms.

Eugene, Ore.

REFERENCES

BATSON, O. V.: Ann. Surg., 112: 138, 1940.
——: Am. J [illegible] Therapy, 48: 715, 1942.
DELORMER, [illegible] Chicago: Year Book Publishers, 1943.
SILVER, C. [illegible] it Dis., 2: 10, 1941.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

STREPTOMYCIN IN GENITO-URINARY TUBERCULOSIS: A PRELIMINARY REPORT OF 10 CASES[1]

CAPT. A. C. ABERNETHY (MC) USN AND LT. H. H. EDELBROCK (MC) USN
From the Department of Urology, U. S. Naval Hospital, Oakland, Calif.

Streptomycin promises to become a valuable adjunct in combating tuberculosis in the human body and especially in the genito-urinary tract. The drug became available to us at the U. S. Naval Hospital in Oakland in the early part of 1946, and we have used it in 10 patients who had failed to respond to other forms of therapy. We are reporting the details of these cases, with the dosage administered and their progress, in the hope that we may add something to the information gradually being accumulated as to the effectiveness of this new drug.

The treatment was based on the following preliminary knowledge:[2]

a) Streptomycin has been shown to protect experimental animals from tuberculosis.[3]

b) It has been shown to prevent the growth of tubercle bacilli in vitro.[4]

c) Postmortem studies of miliary tuberculosis treated with streptomycin have shown healing of kidney and bladder lesions.[5]

d) Up to 86 per cent of the streptomycin given is excreted by the kidneys in an effective state.[6]

e) Studies of streptomycin concentration have revealed high levels of the drug in the renal parenchyma.[6,7]

The use of higher dosage than that given by previous investigators was suggested by the fact that many felt that their failures might be due to inadequate or too brief administration. No patient, however, received more than 400 grams of streptomycin. The intramuscular route was chosen both for its convenience and for the ease of maintaining relatively constant blood levels if the drug was administered at intervals of 3 hours. Since the use of choline chloride[8] was thought to have been a significant factor in the treatment of a case of arrested miliary tuberculosis in this hospital, we have used it in all the cases where the resultant nausea was not too severe.

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, British Columbia, April 19, 1948.

[2] Waksman, S. A. Antibiotics and tuberculosis. J. A. M. A., **135**: 478–485, 1947. (The article contains a comprehensive bibliography.)

[3] Feldman, W. H. and Hinshaw, H. C.: Streptomycin; effects on experimental tuberculosis in guinea pigs. Proc. Staff Meet., Mayo Clin., **19**: 593–599, 1944.

[4] Schatz, A., Bugie, E. and Waksman, S. N.: Streptomycin, a substance exhibiting antibiotic activity against gram positive and gram negative bacteria. Proc. Soc. Exper. Biol. & Med., **55**: 66–69, 1944.

[5] Bagenstoss, A. H., Feldman, W. H. and Hinshaw, H. C.: The effects of streptomycin on pathology of generalized miliary and meningeal tuberculosis. Proc. Staff Meet., Mayo Clinic, **22**: 265, 1947.

[6] Adcock, J. D. and Hettig, R. A.: Absorption, distribution and excretion of streptomycin. Arch. Int. Med., **77**: 179–195, 1946.

[7] Hinshaw, H. C. and Feldman, W. H. Streptomycin, summary of clinical and experimental observations. J. Pediat., **28**: 269–274, 1946.

[8] Godward, A. C. Jr. Streptomycin and lipotrophic agents in miliary tuberculosis. Am. Rev. Tuberc., **55**: 412, 1947.

SUMMARY OF CASES

Case 1. A 29 year old man was admitted in February 1946, with bilateral tuberculous epididymitis and tuberculosis of the prostate and left testicle. Soon after admission the left testicle, epididymis, and spermatic cord were excised up to the level of the internal inguinal ring. We also removed the right epididymis. Persistent postoperative sinuses, draining pus laden with tubercle bacilli, developed in the right scrotal and left inguinal regions.

Six weeks after operation streptomycin therapy was begun at the rate of 0.4 gm. every 3 hours, and was continued for 1 month, 100 gm. being administered. The sinuses closed during the first 15 days of treatment. The sedimentation rate, blood count, and microscopic urinary findings returned to normal. After 60 days he gained 20 pounds and guinea pig studies of the urine were negative for tuberculosis. After 5 months of bed rest he was sent home.

Seven months after the streptomycin had been stopped he began to develop clinical signs of increased prostatic involvement. The sedimentation rate was again elevated and a guinea pig inoculation with the urine was positive. He was readmitted to the hospital.

Additional streptomycin (300 gm.) was given at the rate of 0.2 gm. every 3 hours. The sedimentation rate returned to normal and the symptoms disappeared. Guinea pig tests of the urine became negative after 20 gm. of the drug and have remained so for the 12 months since cessation of treatment. The patient suffered mild dizziness during the time that the drug was being administered, but this subsided when it was stopped. He received choline chloride only 2 days because of marked nausea.

Case 2. A 28 year old Italian man had lost his right kidney for tuberculosis elsewhere in 1942. He continued to suffer intermittent dysuria, frequency, and diminished urinary stream, increasing in severity until his entrance into the hospital in December 1946.

Examination showed dense stricture of the pendulous urethra, probably tuberculous, and extensive tuberculosis of the bladder. The exact status of the remaining left kidney could not be determined by excretory urography because of the low function. The nonprotein nitrogen was 60 mg. per cent.

A suprapubic cystotomy was done and streptomycin therapy instituted at the rate of 3.2 gm. daily. After 1 month the dosage was reduced to 1.6 gm. daily and continued until 400 gm. had been given.

In spite of treatment he continued to run a febrile down hill course, and after 2 months developed complete anuria with signs of ureteral obstruction. An emergency nephrostomy was done, and at operation the kidney was found to be about 75 per cent destroyed by two large abscesses. The nonprotein nitrogen which had been up to 225, dropped to 60 again after the operation. He excreted 2000 cc urine daily and seemed generally slightly improved. However, the nonprotein nitrogen gradually rose again and he progressed to extreme cachexia, uremia, and death on May 21, 1947. Autopsy revealed far advanced tuberculosis remaining in the urinary tract, lungs, liver, and spleen. There was little evidence of retardation or healing of the lesions. This patient became totally deaf during the administration of the first 100 gm. of streptomycin. Only mild dizziness was noticed. He also could not tolerate the choline.

Case 3. A white man of 26 had developed painful swelling of the left testicle in July 1945. This had been incised and continued to drain for 1 year, after which the testicle and cord were removed and the wound healed. In December 1946, the right testicle became painful and swollen and he was first admitted to our hospital. Both the urine and the pus aspirated from the scrotum were positive for tuberculosis. Retrograde urinary tract investigation was not thought advisable, and other studies failed to locate a lesion in the urinary tract. No abnormalities were palpated in the prostate and vesicles.

The scrotum and the epididymis were widely incised for drainage and streptomycin therapy was begun, 0.4 gm. every 3 hours. After 10 days one dram of the 25 per cent elixir of choline chloride was given daily. The wound was completely healed by the fourteenth day. After 1 month the amount of streptomycin was dropped to 0.3 gm. every 3 hours, at which rate it was continued until 400 gm. had been given. He showed transient dizziness from the eighteenth to the twenty-fifth day.

His kidney function, as measured by phenolsulphonphthalein, was normal and remained so. He was discharged on May 10, 1947, but has been rechecked every month. The urine has remained entirely normal, the sedimentation rate has stayed down, and guinea pig tests of the urine have been negative for tuberculosis.

Case 4. A white man of 24 had been treated elsewhere about 1943 for tuberculosis of the left kidney, prostate, and left epididymis. The latter had been removed, and after 18 months of treatment he had returned to his home. He was first admitted to our hospital in October 1946, because of hematuria. The studies showed tuberculosis of the left kidney and ureter, the bladder, prostate, and the left hip. Two weeks after admission a left nephrectomy was done, and 2 weeks later the left ureter was removed. Drainage from the wound followed the second operation, and he ran a toxic course, with temperature to 103 F. daily, and for 6 weeks failed to respond to the ordinary supportive treatment.

On December 4 streptomycin was started with a dose of 0.4 gm. every 3 hours. His condition improved and the fever decreased so that in 6 weeks he was afebrile. The sinuses healed promptly. He showed mild transient dizziness from the eighteenth to the thirtieth days of treatment. After 6 weeks the dose was reduced to 0.2 gm. of streptomycin every 3 hours, and 1 dram of the elixir of choline was given daily. He received a total of 400 gm. of streptomycin.

He is now free of symptoms referrable to the genito-urinary tract. The prostate feels normal. The urine is microscopically normal. The sedimentation rate is down, and guinea pig inoculations of the urine have been negative. He has gained 25 pounds in weight.

The left hip remained unchanged radiographically throughout the treatment and he complained of mild persistent pain there. The orthopedists decided on surgery of the joint, from which he is now recovering in a full body cast.

Case 5. A 52 year old white man in 1919 had the left testicle, epididymis, and cord removed for tuberculosis. In 1934 his prostate was drained perineally for tuberculosis, and in 1940 a tuberculous left kidney was removed.

He was first admitted to this hospital on March 3, 1947, with evidence of extensive tuberculosis of the prostate and bladder. Nodules were also present in the remaining testicle and epididymis. Excretory urograms failed, however, to demonstrate any disease in the remaining kidney and ureter.

Streptomycin treatment was begun on April 1, 1947, at the rate of 0.4 gm. every 3 hours. On the eighteenth day severe dizziness appeared and has persisted in a marked degree. He could not tolerate choline. However, after the tenth day of treatment his bladder symptoms sharply diminished. The sedimentation rate and blood count were elevated, and the urine full of pus, for 2 months. Guinea pig test of the urine was positive after he had received 50 gm. of streptomycin, but became negative after 250 gm. At this point he left the hospital without consent. His symptoms were improved, but the physical findings were unchanged except for some improvement in the prostate. The patient was reexamined in November 1948; all criteria for persistent tuberculous activity were negative.

Case 6. A 23 year old white man had had bilateral epididymectomy elsewhere for tuberculosis. In July 1946, he developed a painless rectal sinus which drained intermittently until his initial entry into this hospital in January 1947. The drainage from the sinus contained tubercle bacilli, and the proctologist found extensive ulceration of the rectal mucosa. The prostate was an irregular nodular mass, fluctuant in places, continuous with the vesicles. The urine was loaded with tubercle bacilli, but the intravenous urograms showed no upper urinary tract disease.

On March 18, 1947, streptomycin was begun, 0.4 gm. every 3 hours. Ten days later the elixir of choline was started, 1 dram daily. After 100 gm. streptomycin had been given the dose was reduced to 0.2 gm. every 3 hours. He received a total of 400 gm.

The rectal sinus and mucous membrane now appear healed, and the prostate feels normal. He has no symptoms. The sedimentation rate did not become normal until 2 weeks after the drug was stopped. The urine is entirely clear, and guinea pig tests have been repeatedly negative every 6 weeks since he had 100 gm. of the drug. His kidney function remains normal and he has gained 18 pounds. He was discharged from the hospital July 15, 1947, but examination and guinea pig tests have been normal every month since that time.

Case 7. A 29 year old woman had the right kidney removed for tuberculosis in our hospital in 1944. Because of continued bladder symptoms the ureteral stump was removed the next year. The symptoms, however, were progressive, and she made the rounds of several large clinics without obtaining relief. She stated that no one had been able to catheterize the ureter of her remaining kidney.

She re-entered the hospital in November 1946, suffering from marked weight loss, night sweats, and marked urinary frequency both day and night. Excretory urograms showed dilated calyces of the remaining kidney and apparent erosion of the lower calyx. The ureter was dilated, fixed, and tortuous, and the bladder markedly contracted. The urine was loaded with tubercle bacilli.

Streptomycin was started December 1, 1946, giving 0.4 gm. every 3 hours. A month later the dosage was cut to 0.3 gm. every 3 hours, and after another month to 0.2 gm. The total received was 400 gm. One dram of elixir of choline was given daily with the last 200 gm. of streptomycin. On the twentieth day of treatment she developed mild vertigo, which persisted but was never severe.

Her urinary frequency began to diminish after she had received 50 gm. of the drug. She now voids about every 4 hours and has no pain. Her sedimentation rate declined, but became normal only after the close of treatment. Her appetite improved and she gained 28 pounds. Temperature and pulse began to recede after 250 gm. of the drug, and gradually became normal. The excretory pyelogram remains essentially unchanged. No acid fast bacilli have been found in the urine since the fifteenth day of treatment. Guinea pig studies became negative on the urine after 100 gm. of the drug and have remained so. The kidney function is normal. She was discharged from the hospital in June 1947, and has remained clinically well.

Case 8. A Chinese man, 24 years old, was admitted August 8, 1947. His left kidney had been removed for tuberculosis a year before. His present complaint was increasing frequency and dysuria, with intermittent hematuria for 6 weeks. Sedimentation rate and blood count were normal. The urine contained blood and was heavily laden with tubercle bacilli. Cystoscopy revealed diffuse inflammation of the trigone and an ulcer near the right ureteral orifice. Excretory urograms did not demonstrate disease of the right kidney or ureter.

In September 1947, streptomycin was begun at the rate of 0.4 gm. every 3 hours, until 120 gm. had been given. After receiving 50 gm. he was symptom free, but the urine still contained pus and blood. After 100 gm. the urine was completely normal. The bacilli could no longer be found and guinea pig inoculation was negative. Repeated at 6 week intervals, they have remained negative. Cystoscopy shows the bladder healed, and the sedimentation rate and phenolsulphonphthalein tests are normal.

Because of these findings and because of severe vertigo, the streptomycin was stopped after 170 gm. had been given. The patient still complains of slight dizziness and his vestibular apparatus shows no caloric response. Two months after treatment he returned to his work as a university student.

Case 9. A 35 year old white naval officer had been under observation for pulmonary tuberculosis during 1945 and 1946, but had returned to duty with apparently arrested lesions. In July 1947, he began to lose weight and developed fever, frequency, dysuria, and pyuria. He was admitted July 21, 1947, at which time he showed evidence of weight loss, tenderness in the left flank, and a boggy nodular prostate. His urine showed numerous blood and pus cells. Sedimentation rate was 21 mm. in 1 hour. Blood count and hemoglobin were normal. The urine contained many acid fast bacilli. Chest films showed no change from the previous year, and the sputum was negative for tuberculosis. Intravenous urograms showed a bifid left renal pelvis, loss of cupping of the terminal calyces, and a diffuse mottling extending into the parenchyma in the lower pole The left ureter appeared rigid, serrated, and slightly dilated Cystoscopy showed a single tiny ulcer just above the left ureteral orifice, and mild injection of the trigone Guinea pig inoculations with urine from the bladder and left kidney were strongly positive

Streptomycin therapy began August 8, 1947, with 0 4 gm every 3 hours Two weeks later cystoscopy showed the ulcer already healed The urine, however, was still full of acid fast bacilli On August 19, after 32 gm of streptomycin had been given in 10 days, a left nephrectomy was done There was a caseocavernous abscess 2 cm in diameter in the upper pole, walled off from the calyx A similar abscess in the lower pole had ruptured into the minor calyx, and the pelvic wall was involved Sections showed tuberculosis throughout the kidney, and guinea pig inoculation with the pus demonstrated viable bacilli Streptomycin was continued after the operation and the wound healed per primam

After receiving 20 gm of streptomycin he became moderately dizzy and continued so After a month of treatment the dosage was reduced to 2 4 gm daily, which was continued until 400 gm had been given He now feels normal except for the moderate dizziness, which is subsiding Cystoscopy shows no disease in the bladder and the prostate feels normal Guinea pig tests of the bladder urine are normal, as are other laboratory tests He could not tolerate choline

Case 10 A 27 year old white man was admitted December 17, 1946, with the typical bladder symptoms of tuberculosis The urine was loaded with blood and pus cells and many tubercle bacilli were found on smears and by guinea pig tests Sedimentation rate was elevated Cystoscopy showed many hemorrhagic areas about the left ureteral orifice, but no ulceration Excretory urograms revealed a normal right kidney and ureter, but dilatation of the left renal pelvis and erosion of all the minor calyces The left ureter was also typically involved

On December 30, thirteen days after admission, the left kidney was removed, and 2 weeks later the left ureter Operative specimens confirmed the diagnosis He ran a febrile postoperative course, frequently up to 103 F, and for 6 weeks both wounds drained pus His temperature then subsided, though the urine still contained pus and tubercle bacilli, and 2 months after operation he went home under the care of a private urologist

He was re-admitted August 6, 1947, because of increasing bladder symptoms and gross hematuria External examination revealed nothing except the well healed operative scars, but at cystoscopy we found two large ulcers near the dome of the bladder, each about 1 cm in diameter, and some injection of the trigone Laboratory studies showed hematuria and pyuria, with acid fast bacilli present in the urine sediment and on guinea pig tests The sedimentation rate was elevated The excretory pyelograms revealed an apparently normal right kidney and ureter

On August 12, 1947 streptomycin was started at the rate of 0 4 gm every 3 hours He showed a transient dermatitis from the eighth to the twelfth day of

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

UTEROVESICAL FISTULA[1]

CARL E. BURKLAND

Uterovesical fistula is a rare condition in which urine dribbles through the cervix into the vagina. The present rarity of reports of this type of fistula is a tribute to the great improvement in obstetrical and surgical judgment and technique during the past twenty-five years. Many cases were reported in the medical literature of the nineteenth century but a gradually lessening number in the first part of this century. Neugebauer in 1889 published a résumé of cases on record at that date, 165 in number. In 1901 Sarabezolles published an account of 36 additional cases. Following his report many cases were recorded up to 1923; since that date I have found record of only 15 cases.

Uterovesical fistulas, like those between the bladder and vagina, are the result of accidental injury in obstetrical, gynecological or urological procedures, radium therapy, or of perforation resulting from inflammatory or neoplastic disease of the bladder or uterus. They are most often incurred during prolonged labor from compression of the bladder wall by the arrested presenting part. The bladder becomes firmly compressed between the child's head and the symphysis pubis, thus causing a devitalization of an area of vesical tissue with subsequent necrosis and sloughing which leaves a permanent defect. The uterine opening of the fistula is usually found in the cervix, rarely in the corpus uteri. The fistula usually opens into the posterior portion of the bladder near the midline. Most of the cases reported are in multipara and in women with contracted pelves.

The symptoms are similar to those of vesicovaginal fistula. Leakage of urine from the vagina is the chief complaint; frequency, dysuria and sometimes suprapubic distress and hematuria follow. Urine may drip continuously from the external os of the cervix but more often there is a valvelike action in the fistulous tract so that the flow of urine occurs only when the bladder becomes full or the pressure of an accumulated pocket of urine opens the cervix. The incontinence may thus be intermittent or continuous. Burr has reported a case in which the entire menstrual flow came from the bladder with no vaginal bleeding. Hess reported a case of unilateral fused kidney in which a catheter, passed through an assumed third ureteral orifice, emerged from the cervical canal through a uterovesical fistula. The patient had no objective or subjective symptoms of the condition.

The diagnosis is made from the history of incontinence, and from vaginal and cystoscopic examination. At times cystography may be of help although this was not true in our case. The appearance in the cervical os of a dye such as methylene blue or mercurochrome injected into the bladder is definite evidence of a communication between the two organs. At cystoscopy, one can often see on the posterior surface of the bladder and usually in the midline, an irregular or slit-like opening which may be surrounded by a small area of congested mucous membrane. The remainder of the bladder may be normal or show diffuse congestion. In some cases a ureteral catheter can be passed through the vesical opening of the fistula and emerge from the cervix. When the vesical end of the fistula is of a valve-like nature its presence may be difficult to detect. It may be necessary to place the patient in the knee-chest position before urine or dye can be seen to flow from the cervix.

---

[1] Read at annual meeting, Western Section, American Urological Association, Victoria, B. C., April 20, 1948.

The differential diagnosis involves a consideration of vesicovaginal fistula, ureterovaginal fistula, incontinence due to injury of the urethral sphincter, extravesical opening of a duplicated ureter, and overflow incontinence from an atonic bladder. If the fistulous opening is small the patient may void some urine naturally, leading to the erroneous conclusion that the fistula is ureterovaginal in type. In none of the above conditions will dye injected into the bladder be seen to flow from the cervix.

The natural tendency of the fistula is to close, rarely spontaneously and completely, by granulation and cicatrization with contraction of its margins. Sims, Brodhead and a few others have reported cases of spontaneous closure of a uterovesical fistula. The treatment usually required, however, is closure of each end of the fistula separately. If many adhesions have formed and the fistula has been present a long time, there may be great difficulty in dissecting the cervix free from the bladder wall.

Many methods of repair have been reported. Either the transperitoneal or vaginal approach may be used, largely depending on the height of the fistula in the cervix or uterus. Some operators feel that the abdominal exposure gives a much better mobilization of the bladder and uterus, although by the use of deep lateral perineal incisions or the Schuchardt incision good exposure may be obtained by the vaginal route. In the abdominal approach the fundus of the uterus is grasped and retracted upward and backward, while the bladder is displaced forward. The vesico-uterine peritoneal reflection is then divided transversely and the bladder and uterus are separated until the fistulous tract is crossed, both ends exposed and closed. In the vaginal approach the best procedure is to expose and suture the vesical and uterine aspects of the fistula through the temporarily transversely divided anterior vaginal fornix after curetting the fistula.

Another plan is to denude and suture the fistula through the temporarily slit cervical lips after curetting the course of the tract. As a measure of last resort an hysterostomaclesis can be done. This necessitates closure of the cervical canal and conversion of the vesical and uterine cavities into one common receptacle. The patient will then menstruate through the urethra.

For a successful result by any method there must be adequate exposure, wide and free mobilization of the bladder, the free release of adhesions and scar tissue about the fistula, separate suture of uterus and bladder, and catheter drainage of the bladder. Diversion of the urinary stream by suprapubic cystostomy or by the use of an indwelling urethral catheter, preferably the former, is imperative. The use of the prone position with the patient on a Bradford frame is very helpful in keeping the urine off the suture line and securing an early, good closure of the wound, thus preventing a recurrence of the fistula. The use of vitamins, especially vitamin C, and the use of sulfonamide drugs and penicillin or streptomycin pre- and postoperatively will aid in controlling infection and in wound healing. The chances of successful operative repair are good except in those cases in which the fistula is due to malignant disease or accompanied by very extensive loss of tissue.

Gottlieb successfully treated a case of uterovesical fistula by passing an electrode into the fistulus tract and coagulating the tract by slowly withdrawing the electrode with the current on. Gann reported the healing of a fistula following three applications of radium inserted into the uterine cavity.

CASE REPORT

Mercy Hospital No. 115910. Mrs. M. L. D., a 36 year old white woman, was admitted to the hospital complaining of intermittent leakage of urine from the vagina following the delivery of her last child 4 months earlier. Her general past health had always been good except for poliomeylitis as a child and diphtheria at 20 years of age, from both of which she recovered with no residual defects. She had had no serious injuries or surgical procedures and had undergone seven pregnancies with six children living and well. Induction of labor and forceps delivery was necessary for the birth of her sixth baby which was stillborn. For some time after the birth of this baby she was bothered with periods of incontinence of urine. These ceased however and did not recur until after the present delivery.

The patient was delivered of a male child, with a fairly large head, by podalic version and extraction. Urinalysis before delivery had revealed many pus cells and gram-negative bacilli and gram-positive cocci. The course was rather stormy for the first 2 days after delivery with fever, rapid, weak pulse, and abdominal distension which required Connell suction for relief. Improvement followed the administration of penicillin for 6 days, and the administration of sulfadiazine for another 6 days. On the eighth post-partum day her temperature was elevated to 102.6F. It continued elevated for 5 days, and then became normal.

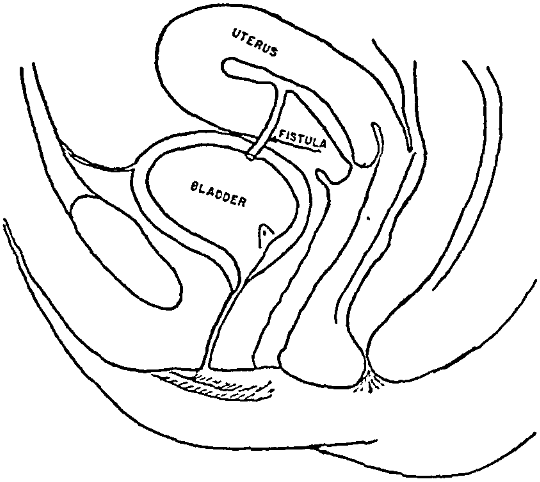
Following delivery the patient was incontinent, though she voided small amounts at times. Voiding was accompanied by burning and distress. For a few days there was some pain in the lower left quadrant of her abdomen. By the tenth and eleventh post partum days slightly larger amounts were voided but incontinence was still present. The patient felt that urine was dribbling from the urethra. There was no mention on her chart of any vaginal drainage of urine. I saw the patient on the fifteenth post-partum day lying in bed in no distress; the abdomen was soft and no masses or organs were palpable. The urethral meatus was red and inflamed but I noticed no vaginal leakage of urine. I thought the cause of the incontinence was probably a weakened urethral sphincter or overflow incontinence from an atonic bladder and ordered a retention bladder catheter and some prostigmin for 3 days. An x-ray of the abdomen was negative for calculi; a urinalysis showed nothing of note. While the Foley bag catheter was in the bladder for 4 days the patient remained quite dry and felt very comfortable After it was removed she voided well with no incontinence and was allowed to go home Shortly after arriving home, however, incontinence recurred and persisted

I did not see the patient again until she came to my office 3 months later At this time she was able to state that urine did leak from the vagina, but there were days and nights when no leakage occurred Cystoscopic examination revealed no abnormal opening in the bladder Argyrol was instilled into the bladder and a vaginal speculum inserted but no fluid appeared in the vagina Thorough inspection of the vagina revealed no fistulous opening As the patient was being assisted from the examining table, the nurse noticed argyrol leaking from the vagina A week later, cystoscopy showed that the bladder mucosa was less congested but revealed no abnormal opening in the mucosa Argyrol was again instilled into the bladder, and again did not appear in the vagina until the patient got off the table An intravenous urogram revealed normally functioning kidneys and the resulting cystogram showed no leakage or fistulous tract from the bladder or ureter on the anteroposterior or lateral views A week later, during a third cystoscopic examination, a slit-like opening was seen on the posterior wall of the bladder directly in the midline Attempts to pass a ureteral catheter through this opening were unsuccessful We thought that we were dealing with a vesicovaginal fistula, the vaginal orifice of which could not be located Admission to the hospital was advised for further study and treatment No new physical or routine laboratory findings were revealed

Sodium pentothal was given intravenously and the patient placed in a modified knee chest or Kraske position We have found this position helpful in operating upon vesicovaginal fistulas and in operations on the female urethra With the patient in this position mercurochrome (1 per cent) injected into the bladder ran out of the cervix Since attempts to find the orifice of the fistula within the cervix were unsuccessful, we thought that its insertion must be higher in the uterus For this reason the transperitoneal approach was recommended for repair of the fistula in order to obtain good exposure and mobilization of the uterus and bladder

The usual low, midline, abdominal, incision was made and the vesico uterine fold of peritoneum was incised transversely Many adhesions were found between the anterior wall of the uterus and the posterior wall of the bladder After these were freed, a short fistulous tract was encountered running from the region of the lower uterine segment to the posterior wall of the bladder in the midline When this tract was cut across an opening about 1 cm in diameter was found in the wall of the bladder and a slightly larger opening in the uterus (fig 1) The mucosa of the bladder was pale, pouting, and very adherent to the fistulous tract A supravaginal hysterectomy was performed The tissues of the uterus were very friable, *pathological examination of the organ revealed chronic endo* metritis The opening in the bladder mucosa was then dissected free, mobilized, and closed with continuous suture of fine catgut placed in the submocosa The muscularis of the bladder was closed in 2 layers using No 2 chromic catgut and the peritoneum apposed over the entire region. The peritoneum was then dissected from the bladder and a suprapubic cystostomy performed. The abdominal incision was subsequently closed in the usual manner and an indwelling urethral catheter placed in the bladder.

On return from the operating room the patient was placed in the prone position on a Bradford frame to keep urine from the suture line. However, she found it difficult to tolerate this position and after 3 days was allowed to lie on her back. The wound healed well. The suprapubic catheter was removed on the thirteenth and the urethral catheter on the sixteenth postoperative days. Urine was voided immediately with no difficulty and there was no suprapubic or vaginal leakage of urine. She left the hospital on the eighteenth day and has had no trouble since. On frequent office visits the urine has been normal and she has felt very well.



UTEROVESICAL FISTULA
FIG. 1. Site of uterovesical fistula in our case

SUMMARY

A case of uterovesical fistula with vaginal leakage of urine is reported following delivery by version and extraction in a 36 year old, para-7, white woman. The present rarity of the condition is due to the great advance in obstetrical and surgical technique in the last 25 years. The diagnosis was aided by use of the knee-chest position. Transperitoneal closure of the fistula was carried out easily with free mobilization of bladder and uterus. The patient obtained a fine immediate and final result.

1127—11th St., Sacramento 14, Calif.

REFERENCES

BRODHEAD, G. L.: Spontaneous closure of large vesico-uterine fistula. Med. Rec., **98:** 437, 1920.
BULLOCK, H.: Utero-vesico-vaginal fistula. Med. J. Australia, **2:** 709, 1922.
BURR, G. C.: Uterovesical fistula. J. Urol., **41:** 906, 1939.

FRANK, R. T.: Post-operative vesico-uterine fistula. Am. J. Obst. & Gynec., 49: 776, 1945.
GANN, D.: Healing of vesico-uterine fistula after radium. Urol. & Cutan. Rev., 26: 343, 1922.
GOTTLIEB, J.: Zentralbl. f. Gynak., 54: 1090, 1930.
HESS, E.: Unilateral fused kidney with uterovesical fistula. Atlantic Med. J., 29: 780, 1926.
HILL, R. S.: Vesico-uterine fistula. South. Med. J., 2: 641, 1909.
KELLY, H. AND BURNAM, C.: Diseases of the Kidneys, Ureters and Bladder. Philadelphia: Lea & Febiger, 1915, vol. 2.
KIRCHNER, W. C. G.: Sigmoid-uterine and vesico-uterine fistula as a complication of childbirth. Am. J. Obst. & Gynec., 25: 241, 1933.
KNIFE, J.: Vesico-uterine fistula. Am. J. Obst., 58: 211, 1908.
MACKENZIE, D. W.: Vagino-vesical and utero-vesical fistulae. J. Urol., 6: 61, 1921.
PARMENTER, F. J. AND LEUTENEGGER, C.: Utero-vesical fistula. J. Urol., 10: 329, 1923.
RUBINS, A.: Labor complicated by utero-vesical fistula. Brit. Med. J., 1: 96, 1926.
SCHNITZ, E. F.: Bladder fistulae in gynecology and obstetrics. S. Clin. North Amer., 5: 1345, 1925.
SIMS, G. K.: Spontaneous healing in vesico-uterine fistula following labor; report of a case. J. A. M. A., 90: 759, 1928.
WARD, C. E.: Repair of vesico-utero-vaginal fistula. Am. J. Dermat. & Genito-Urin. Dis., 16: 233, 1912.
WILLIAMS, R. J. AND SHAW, A. F. B.: Uterovesical fistula. Brit. J. Surg., 31: 404, 1944.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

MANAGEMENT AND MORTALITY OF PERIURETHRAL PHLEGMONS[1]

JOSEPH G. RIEKERT

From the Department of Urology, Bellevue Hospital, New York, N. Y.

Periurethral phlegmons are usually described as a urinary extravasation; however, urinary extravasation is too broad a term for such and includes all conditions following an injury to the pelvis or perineum. True injuries to the lower urinary tract and perineum will not be described in this paper. Periurethral phlegmon is herewith properly defined as a septic infiltration following urethral infection and obstruction resulting in a urinary extravasation. This condition presents a different picture of onset as compared with urinary extravasation following trauma. The periurethral phlegmon begins as a localized, urethral inflammation proximal to a urethral stricture and in conformity with Campbell's statement: "The phlegmon is always pathologically first a periurethral abscess." Urethral strictures of many years' duration are the main etiological factors in this disease. Rolnick has stated that in about 50 per cent of the cases a sound can be passed and there is no apparent loss of continuity of the urethra. In another 15 per cent the urethra appears intact and although a stricture is present it is amenable to dilatation. In only 25 per cent of the cases is an impermeable stricture present in which there is also an extravasation of urine so the amount of urine extravasated is not as important as the virulent organisms introduced into the tissues.

Nonseptic extravasation is more benign. Wolfer has found that the injection of sterile urine did not produce a phlegmonous process. Therefore the classical fascial barriers of Colles and Buck are usually resistant to uninfected urine or experimentally injected fluids but do not resist the infected urine escaping behind the urethral stricture or through the periurethral abscess. The malignant, septic character of the disease is often due to associated anaerobic bacteria including the anaerobic gas forming bacilli. The most commonly encountered organisms are the streptococcus and the Hemolytic staphylococcus and often occurring in combination with the colon bacillus and the gonococcus. The toxemia of the patient with phlegmons is partially caused by the widespread thrombosis and thrombo-phlebitis with gangrene and partially by the organisms involved, but it is caused in part by the extremely wide contact with the tissues. Despite the outstanding thrombo-phlebitis characteristic of the disease, death by pulmonary emboli is rare.

It is about the anatomical barriers that at first limit and then guide the spread of the infection I now wish to describe briefly. Colles' fascia is the deep layer of the superficial perineal fascia. By fusion with the inferior layer of the triangular ligament it attaches in front to the pubis and laterally to the ischiopubic rami and as far back as the ischial tuberosities and then curves forward enclosing the bulb and superficial perineal pouch to become continuous with the dartos of the scrotum and Scarpa's layer of the abdomen. It is then seen that the superficial perineal pouch contains the bulb and bulbous urethra and as most strictures occur in this area and the infection breaks through here into the superficial perineal pouch, Colles' fascia becomes the most important barrier. In our series of cases to be mentioned, over 90 per cent started in the superficial perineal pouch. The other barriers are Buck's fascia which surrounds the penis and may delimit an infection started in the pendulous portion of the urethra. These infections rarely secondarily invade the scrotum and perineum. Finally the triangular ligament, or the urogenital diaphragm as it is often called, would guide an infection starting from the membranous and prostatic urethra. Infections originating in the membranous urethra usually rupture through the superficial layer of the triangular ligament and then follow Colles' fascia. Rarely they break through the deep layer of the triangular ligament into the pelvis. They then may dissect the peritoneum from the bladder and pass into the space of Retzius or may progress posteriorly into the ischiorectal fossae and may include the buttocks and inner, upper aspect of the thighs. This type when first seen may appear to be a perirectal or ischiorectal abscess. We have had 15 cases in which the rectal extension was more marked than the genital. However, a careful history will usually show urinary troubles. In 180 cases only 5 failed to give a substantial urinary history.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 20, 1948.

The patient with a periurethral phlegmon will usually have had urinary difficulties for years and may have had one or more attacks of acute retention. The weakened, eroded, infected area in and about the stricture gives away and septic urine begins to infiltrate the tissues. The patient will often complain that he felt a sharp sensation of "something giving away" as he strained to urinate. He is usually admitted twelve to twenty-four hours later in a stuporous or toxic condition with a history of malaise, fever, chills, prostration and dehydration. He usually shows a swollen, edematous and even gangrenous scrotum with swelling in the perineum and redness of the skin starting to involve the suprapubic area.

External urethrotomy and drainage is the operation of choice for the following reasons:

1) The urinary obstruction incident to the stricture is relieved and the fundamental cause of the infection is thereby corrected.

2) The infected periurethral tissue is provided with drainage.

3) The dependent position of the drainage favors complete emptying of the bladder.

4) It has been shown that Colles' fascia guides 90 per cent of the infections and as the extension is usually to the abdomen due to the fact, anatomically, that Colles' fascia is continuous with Scarpa's layer, the infection then is superficial, really subcutaneous. A suprapubic cystotomy performed through this infected tissue would introduce the virulent organisms into the deeper, uninfected tissue under the rectus sheath.

I make these points because in some institutions suprapubic cystotomy is done by choice. We do external urethrotomies on all our cases. In the last 180 cases external urethrotomies were done in 176 instances. In the remaining 4 cases it was impossible to pass a filiform as a guide to a urethrotomy so a suprapubic cystotomy was performed. In each of these 4 cases, however, external urethrotomy had to be performed later to establish continuity of the urethra.

External urethrotomy also requires a widespread incision and drainage opening up to and beyond the infected areas. The attachment of Colles' fascia to the fascia lata usually prevents spread down the thighs. Circum-anal and gluteal spread is common. The scrotum is almost always involved but very often the penis is protected by Buck's fascia. Parallel incisions through the skin and subcutaneous tissue to the muscle of the abdomen may be necessary and carried as high as the infection spreads, in some cases we have had to carry the incision to just below the axilla. Counter drains connect the incisions and the entire area is packed open with hot potassium permanganate dressings. The scrotum requires special attention in advanced phlegmon. It is often bivalved and the testicles are completely isolated and wrapped in gauze saturated with potassium permanganate. The inguinal canals are opened and in most cases the gangrenous scrotal skin has to be excised. The necessity for wide radical incision and drainage cannot be overemphasized especially when crepitation is felt under the skin, otherwise several hours after surgery the crepitation will be noticed above the incisions and the wounds will have to be reopened. In 12 cases we have had to subject patients to further incision and drainage after what was considered to be adequate drainage. "A timorous incision is the patient's death warrant." (Keyes)

In cases showing crepitation, gas antitoxin should be used and we have given individual cases over 20 therapeutic doses. The mortality in cases where culture was proven to be B. welchii is very high. The whole incised area is kept soaked in potassium permanganate solution postoperatively and allowed to close only after the area looks clean. The external urethrotomy tube is removed when the perineal area has healed in and replaced with an indwelling catheter to close the defect in the urethra. Plastic surgery is often necessary to close the defect in the urethra which has sloughed from gangrene and to cover the testicles after gangrenous scrotal skin has been excised.

Those who object to external urethrotomy and exposure of the testicles state that this is deforming and results in a long stay in the hospital to correct these defects. However, in a disease with such a high mortality, time in the hospital is not to be considered when incising the infected areas. Performing a suprapubic cystotomy will not save time as 60 to 85 per cent of these phlegmons have strictures, most of these of small caliber and the cystotomy sinus is not apt to close without urethral dilatation or long inlying catheter. This is also what is done to close the defect in the urethra from an external urethrotomy without the additional benefit of the strictures being dilated perineally as in a urethrotomy. After discharge from the hospital urethral dilatations must be continued and failure to do so has resulted in several cases returning after one or two years with a new periurethral abscess or phlegmon.

One typical advanced case on admission showed a huge, edematous scrotum with an area 4 by 4 inches of black, gangrenous skin. Crepitus was felt over the remainder of the scrotum, extending over both iliac crests well into the left flank and, most unusual, down the left leg to the ankle. He was treated in the manner already described with an external urethrotomy and incision and drainage down the left leg, over the buttock and up the abdomen. Because the culture yielded B. coli, Streptococcus hemolyticus and B. welchii he was given continuous doses of penicillin and gas antitoxin. The wounds healed, all crepitation disappeared but on the thirteenth postoperative day cardiac decompensation developed, and the patient expired. The final nonprotein nitrogen was 112.

In the Department of Urology at Bellevue Hospital we have treated over 800 cases of periurethral abscess and periurethral phlegmon in the past 25 year period. The cases used in this study total 372, of which 194 are classified as periurethral abscess and 178 as true phlegmons, in that they had already broken down the fascial barriers. To evaluate the relative merits of sulfonamides and penicillin on the mortality of the disease, the study is divided into two 6 year periods. Series 1 prior to the use of chemotherapy and penicillin, and in series 2 where sulfonamides and penicillin, together or separately, were used on all cases. See tables 1 and 2. From this it can be seen that sulfonamides and penicillin carry little importance in periurethral abscesses if a prompt external urethrotomy is performed as the mortality in each series is zero. In periurethral phlegmons, sulfonamides and penicillin have played a significant role in lowering the mortality from 38 per cent to 20 per cent as the surgery was the same in both series.

TABLE 1

Series 1, 1932–1938 *No sulfonamides or penicillin*

Periurethral abscess	89	deaths	0	mortality	0%
Periurethral phlegmon	103	deaths	39	mortality	38%

Series 2, 1940–1946 *Sulfonamides and Penicillin*

Periurethral abscess	105	deaths	0	mortality	0%
Periurethral phlegmon	75	deaths	15	mortality	20%

The causes of death are listed to show that chemotherapy has lowered the chief cause of death, toxicity and septicemia, to a much lower rate. Before chemotherapy the majority of patients died of septicemia, often with positive blood cultures of Streptococcus hemolyticus and Staphylococcus aureus.

Table 3 illustrates the fact that one-third of all mortalities occur on the first postoperative day. These patients were often moribund and the disease so advanced that emergency surgery and all supportive measures are of little avail. All periurethral infections, even what appear to be simple abscesses, should be treated as emergencies and are operated on within 24 hours or less. The value of this policy is borne out in the mortality record between periurethral abscesses and periurethral phlegmons. Failure to operate upon a periurethral abscess may result in a periurethral phlegmon by the next day.

The mortality figures of various reporters are presented in table 4.

One final thought should be mentioned. Many of these cases of periurethral abscess and periurethral phlegmon on admission will have the ability to urinate with what appears to be a good stream and not be in urinary retention, but an external urethrotomy should nevertheless be performed. Although in a few mild cases the patients may recover with an indwelling catheter and simple

TABLE 2. *Causes of deaths in periurethral phlegmons*

Series I	39 deaths	average age 49 years
A. Toxicity and septicemia		27
B. Pneumonia		4
C. Pulmonary infarct		3
D. Heart failure		3
E. Uremia		1
F. Cirrhosis of the liver		1
		39
Series II	15 deaths	average age 56 years
A. Toxicity and septicemia		5
B. Uremia		4
C. Heart failure		3
D. Anesthesia		1
E. Generalized tuberculosis		1
F. Ascites		1
		15

TABLE 3. *Postoperative survival in days*

DAYS	CAMPBELL SERIES (*BELLEVUE 1915–1929*)	SERIES I	SERIES II
	deaths	*deaths*	*deaths*
1	15	10	5
2–5	15	6	2
6–10	10	9	3
over 10	15	14	5
	55	39	15

TABLE 4. *Mortality of periurethral phlegmons*

		cases	%
Before Sulfonamides and Penicillin			
Campbell	1915–1929	135	43
Finestone	1930–1939	32	50
Smith and Finton	1925–1940	133	56
Bellevue Series I	1932–1938	103	38
With Sulfonamides and Penicillin			
Beard	1938–1946	92	25
Bellevue Series II	1940–1946	75	20

incision and drainage, in many cases one will find it necessary to go back later and do a urethrotomy. We have had 10 cases treated only by incision and drainage but in 2 of these cases of periurethral phlegmons the patients died, and these could at all times urinate freely.

CONCLUSIONS

Treatment of periurethral phlegmon begins with prompt radical incision and drainage with diversion of the urinary stream.

External urethrotomy is the operation of choice for diverting the urinary stream.

Sulfonamides and penicillin have resulted in a lowering of the mortality about 15 per cent in our series of periurethral phlegmons.

945 Lexington Ave., New York, N. Y.

REFERENCES

Beard, D. E.: Urinary extravasation. Urol. & Cutan. Rev., 50: 517, 1946.
Campbell, M. F.: *Periurethral phlegmon. Surg., Gynec. & Obst., 48: 382, 1929.*
Eisendrath, D. N. and Rolnick, H. C.: Textbook of Urology. Philadelphia: J. B. Lippincott Co., 1938.
Finestone, E. O.: Periurethral phelgmon. Ann. Surg., **116**: 109, 1942.
——: Urinary extravasation. N. Y. State J. Med., **43**: 1320, 1943.
Smith, H. S. and Finton, R. E.: Urinary extravasation. Urol. & Cutan. Rev., **45**: 481, 1941.
Tashiro, S. and Hinman, F., Jr.: Periurethral and perirectal infections. J. Urol., **57**: 338, 1947.
Wolfer, J. A.: Urinary extravasation. Surg., Gynec. & Obst., **26**: 296, 1918.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DISCUSSION

DR. A. LYNN HERRING (Memphis, Tenn.): Dr. Riekert is to be congratulated upon the clear and concise presentation of his paper and for his worthy contribution to our knowledge of periurethral phlegmons by his study of a large series of cases both before and after the sulfa drugs and antibiotics were available in the treatment of these conditions.

The seriousness of urinary extravasation with resulting phlegmons is best shown by the high mortality and morbidity rates. This condition is seen rather infrequently in private practice today, but to those of us on the charity services of hospitals in the South where there is a large colored population, it is a common sight.

A review of 100 consecutive cases of periurethral phlegmon treated at the John Gaston Hospital, the teaching institution of the University of Tennessee Medical School at Memphis, are included in this report. All of these were given sulfonamides but only 25 per cent had penicillin as it was not available for general use at the time the majority of these patients were seen. There were 36 cases of periurethral abscess with no deaths and 64 cases of periurethral phlegmon with 21 deaths, or a mortality of 33 per cent. Thus, from a comparison of the results reported by Dr. Riekert with 20 per cent mortality when both penicillin and the sulfonamides were used, it appears that penicillin is more effective than sulfonamides in combating periurethral phlegmons.

The etiology is well demonstrated by the fact that in this series the incidence of proved stricture of the urethra was 91 per cent. A history of gonorrhea from one to several times was obtained in 67 per cent. Acute retention of urine was present in 54 per cent, an additional 12 per cent gave a history of difficult urination, and urethroperineal fistulas were present in 8 per cent.

The principal treatment of these patients remains unaltered in that it is surgical. Wide and radical incision and drainage of the involved tissues should be done on an emergency basis and at the same time provision should be made for urinary drainage. In this series 34 per cent had suprapubic cystostomy, 9 per cent had external urethrotomy and 8 per cent had suprapubic cystostomy followed later by a permanent external urethrotomy. Six per cent had had external urethrotomies prior to admission. Other than surgery, treatment should include penicillin and/or sulfonamides, supportive measures such as blood transfusions, adequate hydration, high vitamin intake, hot wet dressings of some mild antiseptic solution to the involved areas and hot sitz baths as soon as the patient is ambulatory.

The phlegmons in this series involved the perineum and scrotum in 32 per cent, the perineum alone in 25 per cent, the scrotum and anterior abdominal wall in 18 per cent, and were limited to the penis alone in 6 per cent. There was perirectal involvement in 3 per cent.

The morbidity of this condition is illustrated by the following:

1) Hospitalization varied from 1 to 138 days for an average of 18 days.

2) Twenty-seven per cent of the patients in this series had two or more admissions with the same diagnosis.

3) Following hospitalization periodic dilatations of the urethra were required for an indefinite period.

In closing I should like to cite 24 cases of periurethral phlegmon treated in 1947 and not included in the above series. All of these had penicillin and sulfonamides, surgical drainage, and suprapubic cystostomy for urinary drainage. There were 2 deaths (one of which was an anesthetic death), a mortality of 8 per cent. This is by far our best year's record in the management of this serious problem.

Dr. Eduardo Castro (México, D. F.): Dr. Riekert is to be commended on this splendid presentation of the management of periurethral phlegmon.

I rise before you only to say that in 1942 I read before this Association a translation of a paper I had published in the Mexican Review of Urology, and in which I spoke about the reduction in mortality obtained at the Hospital Juárez in cases of periurethral phlegmon, from 50 per cent down to 15 per cent, such a lowering being due to the routine use of small transfusions of blood, to supplement the usual measures of ample incisions and diversion of urine, preferably through an external urethrotomy.

Since the advent of penicillin we have had no mortality in 83 cases, treated within a reasonably short time after the onset of the extravasation. Two cases which died in 3 years' time were in the hospital less than 24 hours. The good effect of the transfusions is still further shown by the shortened healing time.

Dr. Joseph G. Riekert (New York, N. Y.): We have found it difficult at Bellevue Hospital to reduce the mortality below 20 per cent, for two good reasons: 1) Many of our cases are so advanced and so moribund on admission, that surgery is done just to give them a fighting chance. One-third of these patients expire the first day, despite transfusions and penicillin and all that can be done. 2) Many of them are hopelessly late cases, and I think until we get earlier cases, our mortality will stay at approximately 15 to 20 per cent.

With the advent of antibiotics, we can clean up the infections. They live several weeks. Locally there is a healing but the nonprotein nitrogen seems to mount and they die of uremia. Whether this is toxic nephritis brought on at the time of the original infection, we can't say, but the infection locally cleans up under the antibiotics, and they die of uremia.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

RETROPERITONEAL CREPITANT CELLULITIS FOLLOWING URETHRAL INSTRUMENTATION: REPORT OF A CASE OF THE CLOSTRIDIAL TYPE[1]

A. FRED TURNER, JR., LOUIS M. ORR AND J. C. HAYWARD

Although gas bacillus infections involving almost every organ of the body have been reported, the urinary tract is so seldom involved that the urologist usually considers this type of infection as a clinical rarity and outside of his field. A review of the literature, however, reveals that such infections are encountered more frequently in urological practice than is generally thought. Moreover, since early clinical diagnosis offers these patients their only hope of survival, it behooves the urologist to become more familiar with the diagnostic signs and symptoms of this entity. In retrospect, our case appears to have been typical in many respects, and the diagnosis of gas bacillus infection could have been made clinically.

Gas bacillus infections have been described following surgery on almost every part of the body. This complication has been reported most often following appendectomy and cholecystectomy and also subsequent to operations where fecal contamination is likely. The relatively few such cases reported following urological surgery do not differ materially from those following other types of surgery. Lazarus was able to find 25 cases of gas bacillus wound infections following kidney surgery, including 2 cases which he reported. Mencher and Leiter reported 14 cases of postoperative anaerobic infections of the urinary tract encountered at the Mount Sinai Hospital during the preceding 11 years. Eleven of these cases were B. welchii infections, and the other 3 were infections by tetanus bacilli.

We were able to find reports of 3 cases in the literature which rather closely resembled our case. Two of these were reported by Dunham in 1897, and one was mentioned by Hotchkiss in a discussion of a paper by Hitzrot in 1912. All 3 of these infections developed after the passage of sounds on the third, fourth, and fifth days respectively after external urethrotomies for strictures. The onset in Dunham's cases was rapid (21 hours after passage of the sound in one and 7 hours in the other). Both were initiated with a chill, and death occurred 33 hours later in one case and 45 hours later in the other. Subcutaneous emphysema became widespread before death in both cases, and in both emphysema of a number of abdominal organs was found at necropsy. B. welchii was cultured from these organs. As for the case mentioned by Hotchkiss, no information was given other than that it "was rapidly generalized and fatal."

CASE REPORT

Mr. J. K., a 42 year old, rather poorly nourished truck driver, was admitted to the Orange Memorial Hospital on May 29, 1947, with overflow incontinence of several months' duration. He was found to have an alkaline urine cloudy with leucocytes, distention of the bladder midway to the umbilicus, and several strictures in the pendulous urethra which permitted passage of LeFort sounds no larger than 16F. On May 30, 1947, an internal urethrotomy was performed with the Riba electrotome and a 24F Foley catheter inserted. His postoperative course was uneventful. Nine days after operation the catheter was removed and the following day the patient was discharged, voiding freely. He then returned to the office every 2 weeks for urethral dilatations.

---

[1] Read at annual meeting, Southeastern Section, American Urological Association, Hollywood, Fla., January 8, 1948.

Six weeks after discharge from the hospital the third dilatation of the urethra was carried out in the office. Ten hours after the instrumentation, the patient was readmitted to the hospital because of fever, chills, malaise, and vomiting. Woven bougies up to size 26F had been passed in the office and noted to be tight, but no unusual difficulty had been encountered in their passage. On admission the patient appeared ill, his temperature was 100.6 F., and his pulse 100, but otherwise the physical examination was essentially negative. Parenteral fluids were administered and 50,000 units of penicillin were injected every 3 hours. For 8 hours after admission his condition seemed slightly improved, but thereafter began to show signs of severe and progressive toxemia, with peripheral circulatory collapse and rapidly mounting temperature, eventuating in death 45 hours after admission. Supportive measures such as blood transfusions, oxygen tent, Levine tube with suction, penicillin, and parenteral fluids seemed to have no effect on the rapidly progressive illness. As the temperature mounted steadily toward its maximum of 108 (fig. 1), the abdomen remained soft, but severe vomiting persisted and was soon accompanied by diarrhea. Blood and mucus appeared both in the vomitus and stools. The Wangensteen suction applied to the levine tube aspirated enormous amounts of gas. Except for the first 12 hours in the hospital, the radial pulse was imperceptible, and the extremities were cold and clammy. Anuria existed throughout the terminal illness, for it was only a few hours before his death when we were able to obtain a few cubic centimeters of urine by catheterization. This urine contained 4 plus albumin and 100 leukocytes microscopically per low power field uncentrifuged. On the day after admission, the white blood count was 15,700 with marked increase in young polymorphonuclears, the hemoglobin was 84 per cent, red blood cells 4,460,000. On the day of his death the blood urea nitrogen was 85 mg. per cent.

Necropsy was performed 4 hours after death. The mucosa of the stomach and that of the colon showed several rather large hemorrhagic areas, and the walls of the colon exhibited crepitus due to emphysema. Numerous, small, thin-walled diverticula, each containing a small fecalith, were found in the colon. The bladder musculature was greatly hypertrophied and in some areas the bladder mucosa was hemorrhagic. The prostate was surrounded by a thick layer of old, dense, inflammatory tissue. A small prostatic abscess was present below the floor of the prostatic urethra. Careful search and dissection failed to reveal any evidence of injury which might have been produced by the passage of bougies. A most striking finding was the stripping up of the entire pelvic peritoneum by numerous tiny, clear, gas filled vesicles, some of which were coalesced (fig. 2). Palpation revealed extensive crepitus of the iliopsoas muscle and of the muscles lining the pelvis. One group of these coalescent vesicles with a

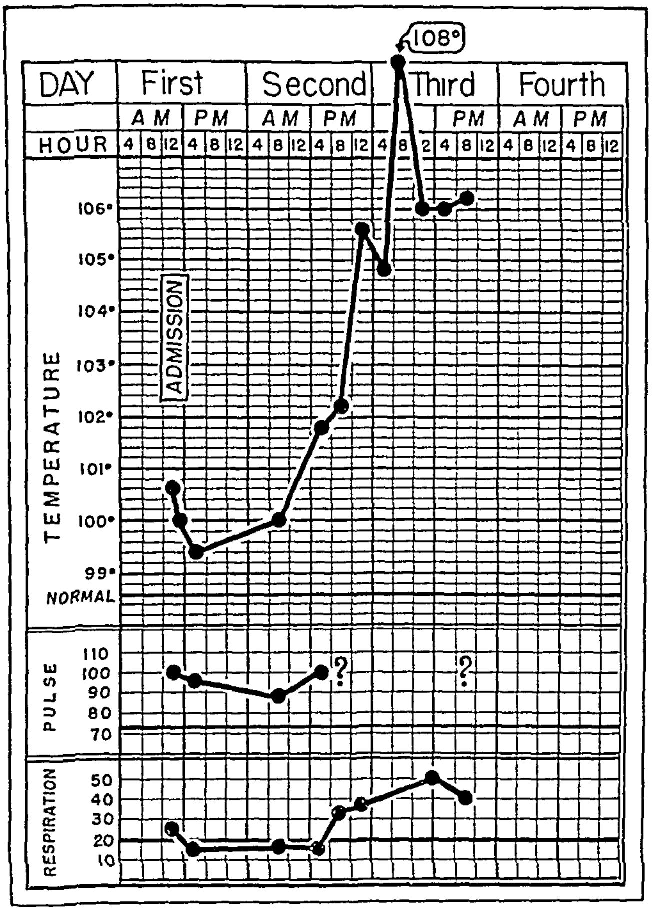


FIG. 1. Showing progressive rise in temperature and early advent of imperceptible radial pulse.

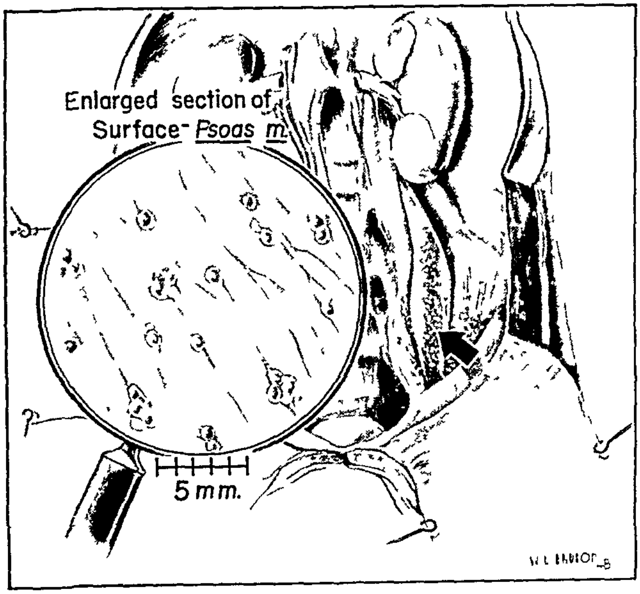


FIG 2

small piece of attached muscle was cultured and B welchii reported The other abdominal organs were grossly normal, but microscopic examination of the liver and kidneys showed parenchymatous degeneration, as might be expected in association with severe toxemia

Microscopic sections from several hemorrhagic areas of the intestinal wall showed extravasation of red cells in the mucosa with disruption and separation of the fibers of the submucosa by fluid and gas.

DIAGNOSIS

Early diagnosis of postoperative gas bacillus infection can be made only through familiarity with the clinical signs and symptoms characteristic of the infection If the diagnosis must await the demonstration of subcutaneous emphysema by eliciting crepitus, the process may have progressed beyond the point at which cure can be expected, and in cases such as ours, the emphysema may be in areas which are not accessible to examination

The classical description of this type of infection by Nason and Starr is essentially one of progressive, irreversible circulatory collapse, with cold, clammy extremities, and temperature increasing progressively to as high as 108 to 110 F Death occurs in about 36 hours

BACTERIOLOGY

Reeves has pointed out that considerable confusion exists at present concerning anaerobic gas forming bacilli This he attributes to the fact that any lesion characterized by gas in the tissues together with gram positive bacilli is considered to be gas gangrene In most reported cases the pathogenic organism has been identified as B welchii on cultural information which has not been presented, or which could be accepted only as presumptive for the organism In other instances, the mildness of the cases in which C welchii is reportedly isolated casts some doubt upon the accuracy of the bacteriological reports As one of the members of the genus Clostridium, of which C tetani and C botulinum are also members, C welchii produces a powerful, necrotizing exotoxin, which lyses red blood cells, causes focal necroses in the kidneys and liver, and causes hematuria and hemorrhages in various parts of the body Our case certainly met all the requirements concerning toxicity of C welchii, but the bacteriological method used could hardly be considered more than presumptive We therefore have chosen to classify our case simply as one of clostridial infection, since further identification of the organism is of more bacteriological than clinical interest

The term "crepitant cellulitis" has been chosen in preference to the more commonly used term "gas gangrene," since it is more descriptive of the actual condition found Gangrene did not exist in our case, probably because its fulminating course with early death from toxemia did not permit progression of the pathological process to this point

The route by which the organism entered the retroperitoneal spaces in the absence of any demonstrable lesion in the urethra is a matter for speculation No proof exists that the passage of bougies actually caused the cellulitis, but it seems the only reasonable explanation. It is usually assumed that such infections metastasize by way of the lymphatics. It seems reasonable to believe that some organisms present in the urethra may have entered the lymphatics of the urethra through microscopic openings produced by the passage of the instruments, and from there been transmitted in this manner to the retroperitoneal lymphatics.

The property of the pathogenic clostridial organisms to lie dormant in previously traumatized tissues for months or years and eventually to become active is illustrated by the not unusual reports of serious gas gangrene following some simple plastic operations.

The specific factors which determine whether or not gas gangrene develops in a wound in the presence of clostridial contamination are not known.

Hendry reports 2 cases of acute gas gangrene with onset almost ten years after the initial wound.

TREATMENT

According to Altemeier, successful treatment depends primarily upon early recognition of the process and early radical decompression by wide surgical incisions. Chemotherapy with sulfonamides and particularly with penicillin are valuable adjuncts to surgery, and the use of adequate amounts of specific antitoxin aids somewhat in the control of the profound toxemia. Daily blood transfusions for the correction of anemia and parenteral fluids are indicated.

Application of oxidizing agents such as zinc or hydrogen peroxide to the infected area when accessible is helpful.

In a case as fulminating and rapidly progressive as the one herewith presented, it is hardly conceivable that any treatment could have been of any avail. Penicillin was administered apparently without effect. Antitoxin would perhaps have been somewhat more effective, since the exotoxin produced by this organism appears to have been the principal cause of death.

SUMMARY AND CONCLUSION

A case of clostridial type of retroperitoneal crepitant cellulitis following the passage of bougies for urethral dilatation has been presented. The clinical picture of overwhelming toxemia with peripheral circulatory collapse, rapidly mounting temperature, and death about 45 hours after the appearance of first symptoms has been described as clinically characteristic of the disease. Diagnosis, made at autopsy, could have been made clinically. Gas bacillus antitoxin administered early may have altered the course of this case.

307 S. Orange Ave., Orlando, Fla.

REFERENCES

Altemeier, W. A.: Postoperative infections. S. Clin. North Amer., **25**: 1200–1228, 1945.

Dunham, E. K.: Report of 5 cases of infections by the Bacillus aerogenes capsulatus (Welch). Johns Hopkins Hosp. Bull., **8**: 68–74, 1897.

Hendry, A. M.: Latent gas gangrene infection. Brit. J. Surg., **17**: 467–472, 1930.

Hitzrot, J. W.: Gas bacillus infection. Ann. Surg., **55**: 624, 1912.

Lazarus, J. A.: Bacillus welchi infections complicating surgical procedures upon the upper urinary tract. J. Urol., **51**: 315–324, 1944.

Mencher, W. H. and Leiter, H. E.: Anaerobic infections following operations on the urinary tract. Surg., Gynec. & Obst., **66**: 677–683, 1938.

Nason, L. H. and Staff, A.: Gas bacillus infection complicating laparotomy. Arch. Surg., **29**: 546–554, 1934.

Reeves, J. R.: Infections by gas-forming anaerobic bacilli: An analysis. J. A. M. A., **104**: 528–529, 1935.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

VESICOCOLIC FISTULA COMPLICATING DIVERTICULITIS. CASE REPORTS[1]

FEDOR L. SENGER

Vesicocolic fistulas are communications which exist between the bladder and the colon. A review of the literature indicates that these are not of sufficient rarity to be classed as medical oddities, but a few of our recent cases have drawn our interest to this problem. These cases and a greater majority of the cases reviewed demonstrate the importance of this condition in the etiological diagnosis of recurrent, intractible cystitis. The underlying pathology is rarely diagnosed on the first visit, but the persistence of the presenting symptoms should always make the urologist suspicious of a minute fistula. The first reported case in the literature was in the second century A.D., in which a patient was described whose urine passed per rectum. In 1888 Cripps published a very complete dissertation on the subject of passing air and feces through the urethra. Since then well over 800 cases have been reported without respect to their etiology.

Etiology of vesico intestinal fistula is variable but it may be divided into four general classes: inflammatory, traumatic, neoplastic, congenital.

In Higgins' report of 328 cases, inflammatory lesions were the etiological factor in 160 cases, diverticulitis being the initiating cause in 92 cases or 57.3 per cent. Rusche and Bacon stated that diverticulitis accounts for approximately 50 per cent of all cases on record of the inflammatory type. Kellogg found that 42 per cent were secondary to diverticulities in a summary of 592 cases. In Dobson and Moir's series, 30 out of 46 cases were due to diverticulitis. Because of this interesting incidence, a discussion of diverticulitis as an etiology in vesicocolic fistula has therefore been undertaken. This is of special import since the incidence of diverticulosis may be on the increase.

Vesico-intestinal fistula occurs more frequently in men than in women in the ratio of 3 to 1. The infrequency in women is possibly due to the interposition of the uterus between the bladder and the rectum, and this acts as a barrier to communication between the two organs. In addition, diverticulitis is of lower incidence in female patients. The condition is most frequent in the sixth and seventh decades. All of our cases were men and the average age was 57 years. The site of the opening of the fistula seems to be most frequently on the left of the fundus and on the posterior wall. The diverticulum usually originates in the sigmoid colon since the sigmoid flexure is involved in 70 to 80 per cent of the cases of diverticulitis.

The pathological chain of events that take place in the diverticulum are, first, an acute inflammatory reaction which results from a filling of the diverticulum with feces and bacteria. The orifice of the diverticulum becomes occluded due to the edema and this is followed by peridiverticulitis and the formation of dense adhesions between the bladder and the bowel. The inflammation may then subside or may proceed to suppuration, rupture and the development of the fistula.

---

[1] Read at annual meeting American Association of Genito Urinary Surgeons, Skytop, Pa., May 12, 1948.

The presenting complaint is usually pneumaturia and soon after, fecaluria. Barnes reports that 90 per cent of his cases presented pneumaturia as a symptom and in 23 per cent there was fecaluria. Both were present in all of our cases. There are symptoms of an acute cystitis which gradually subside and later recur. In addition, there is lower abdominal pain, fever, and other symptoms of diverticulitis depending upon the location and extent. Although pneumaturia ordinarily occurs, it is not pathognomonic of a fistula as it may follow instrumentation or a bacterial fermentation in glycosuria.

A minute colic fistula which permits the passage of gas but not fecal matter into the bladder may defy demonstration for a time. A complete urologic examination is necessary. Cystoscopically, a small, punched-out lesion is usually seen surrounded by an area of marked edema. However, in the more acute phases this cannot be made out due to engorgement. The location of the acute and inflammatory reaction, being usually rather localized, is characteristically seen on the posterior wall of the bladder or fundus in contrast to the usual forms of cystitis which are confined to the trigone or are generalized. Barnes believes that this feature is almost diagnostic in itself since he was able to visualize the fistulous tract in only 6 out of 26 cases.

There are several other diagnostic procedures which may be used. Cystograms may be used, but in our experience, they have usually failed to demonstrate the fistula. Only 3 out of 15 cases in Barnes' series were diagnostic using this method. Barium enemas alone also fail in this respect unless the tract is comparatively large. However, by the combined use of a bladder aerogram and a barium enema, we have been more successful in demonstrating the small fistula. This is accomplished by injecting 8 to 10 ounces of air into the bladder following the administration of the barium enema. After partial evacuation of the barium, the patient is asked to strain down as the post-evacuation film is taken. The contrasting medium then of the bladder outlined against the sigmoid colon will demonstrate the barium entering the bladder. Colored solutions may be introduced into the bladder and recovered in the rectum in some cases.

Proctoscopy alone is universally unsuccessful in visualizing the defect unless it is very large. But the combined use of a colored solution such as methylene blue and injecting it into the bladder, and then direct observation of its exit into the sigmoid is sometimes valuable. In certain instances in spite of all facilities available for diagnosis, exact nature of the lesion in the bowel and the location of the fistulous tract can be determined only at the time of operation.

The treatment is essentially surgical and the consensus favors a preliminary colostomy and then a period of 6 weeks to even 6 months to allow the inflammatory process to subside. During this time the fistulous tract may close spontaneously. In cases of nonhealing, the fistulous tract is subsequently explored, the diseased bowel is resected and the fistula is repaired. The desirability of a temporary suprapubic cystotomy or an indwelling catheter is stressed, following the second stage. Finally, a third operation is the closure of the colostomy.

ture of 103 F. and moderate suprapubic tenderness. Cystoscopy and cystography failed to show any fistulous opening. On the post-evacuation film of the examination with barium enema, there was definite evidence of passage of barium into the bladder through the fistula. There were numerous diverticula visualized in the sigmoid colon. A preliminary transverse colostomy was done on December 20, 1946. On January 13, 1947, the fistula was resected and the vesicosigmoidal opening was closed transversely in double layers. On February 17, 1947, the colostomy was closed and within 3 days gas and feces were being passed per urethram. The patient was discharged and was readmitted on April 25, 1947, and a colostomy was again done. Following a period of 5 months' rest the fistula was resected and in addition, 12 cm. of markedly diseased bowel were resected and an end-to-end anastomosis was done. Six weeks later the colostomy was closed; the patient is now asymptomatic.

Case 3. A 52 year old white man was first seen in March 1941, with complaints of cystitis for 3 months. He gave a history of being treated for diverticulosis since 1938 and, aside from the above, was in good health. Cystoscopy revealed chronic cystitis, for which he was treated by chemotherapy. Except for 3 attacks of pyuria and some suprapubic distress, he was comparatively well until he was seen on October 11, 1946. At that time he was complaining of frequency, suprapubic distress and pyuria of 2 weeks' duration.

On the day of admission, he noticed gas and feces in his urine. At cystoscopy, because of the marked edema and hyperemia, no definite defect could be seen. A cystogram revealed an irregularity in contour in the superior portion of the bladder, but no dye was seen to enter the fistulous tract. Preliminary to the barium enema studies, 200 cc air were injected into the bladder and a definite fistulous connection between the bladder and midsigmoid was seen on examination of the film. Conservative therapy was used in an attempt to heal the defect and, although there was apparent improvement for several months, the symptoms recurred and on November 29, 1947, the patient was admitted to the hospital. A preliminary transverse colostomy has been done and a second stage repair is contemplated following a 3 months' interval.

Case 4. A 59 year old man was admitted to the hospital on April 3, 1941, with a history of frequency, nocturia and intermittent pyuria for about 1½ years. These had occurred in attacks which quickly cleared with bladder irrigation. Ten days before admission another attack occurred with greater severity, and he had noticed burning on urination. The past history revealed that he had been treated for diverticulitis for about 3 years.

On physical examination, lower abdominal tenderness was revealed, but no mass was found to be present. There was chronic prostatitis. Urine examination showed clumps of pus cells and a pure culture of B. coli was grown. Cystoscopy revealed acute, generalized cystitis and moderate prostatic lateral lobe intrusion. There was no evidence of an ulcer or tumor. A transurethral resection was done on April 11, 1941, and 4 days later he developed signs of intestinal obstruction. He was found to be very tender in the right lower quadrant with generalized tympany. The patient was decompressed with a Miller-Abbott

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

RECTO-URETHRAL FISTULA: REPORT OF A SUCCESSFUL REPAIR BY EXPOSURE OF THE FISTULA INSIDE THE EXTERNAL RECTAL SPHINCTER AND WITHOUT A PRELIMINARY COLOSTOMY[1,2]

LEROY J. KLEINSASSER, RALPH SMITH AND OTTO GRIFFIN
From the Departments of Surgery and Urology, Veterans Administration Hospital, Dallas, Texas

Attesting to the frequent failure of the repair of rectourethral and rectovesical fistulas, many methods for the cure of this condition have been proposed. Although any method of repair must stand the test of time, the following case merits reporting. The main features of the repair are the ease of approach to the fistula by a method described by Belt for radical perineal prostatectomy, and the use of an antibiotic, streptomycin, in place of a preliminary colostomy for fecal stream diversion from the operative site.

CASE REPORT

C. L. R., a white man, aged 23, entered the Veterans Administration Hospital, Dallas, complaining of the passage of gas through the urethra and urine through the rectum. He had been wounded by shrapnel 2 years previously, with injury to his pelvis, bladder, and rectum. He had been operated upon twice, and several perforations of the bladder were closed and a cystostomy done. Apparently no attempt was made to close the rectal perforation which he had as a result of the injury. Following this, he first noticed gas passing through his urethra, and after getting up, he noticed urine coming from his rectum. During coitus he failed to expel any semen through the urethra.

The perineum presented no unusual findings. The anal sphincter exhibited good tone. There was evidence of much scarring in the anterior rectal wall. Proctoscopic examination disclosed the patulous orifice of a fistula which entered the lower rectum, anteriorly, 5 cm. above the anal verge and from which clear straw colored fluid could be expressed. The tract seemed to extend through the prostate and seminal vesicle region. A probe could be introduced easily. A No. 21 panendoscope was passed into the bladder on July 22, 1947, and no unusual fidings were noted in the bladder or trigone. The internal vesical sphincter appeared normal. Immediately distal to the internal vesical sphincter, there was a depression on the floor, slightly to the right side, extending back to the verumontanum which was covered with mucous membrane slightly lighter in color than usual. A cystogram did not provide any unusual findings. The

---

[1] Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

[2] Since writing this paper evidence has been presented in the literature that streptomycin given orally is only effective for three days after which escape from its control of bacteria in the colon becomes evident. Sulfathaladine and sulfasuxidine appear more effective for prolonged control of bacterial flora in the gastro-intestinal tract.

persistent cystitis. The most prominent complaint is pneumaturia and, when accompanied by fecaluria, it is diagnostic. The ulcer is not always seen cystoscopically, but an area of local edema is usually present in the fundus of the bladder. Barium enemata may be diagnostic in a very high percentage of cases when combined with bladder aerograms. The treatment of choice is a 3-stage surgical repair with long intervals between stages.

144 Joralemon St., Brooklyn, N. Y.

REFERENCES

Barnes, R. W. and Hill, M. R.: Intestinovesical fistula. J. A. M. A., **133**: 456, 1947.
Cripps, H.: The Passage of Air and Feces Through the Urethra. London: J. and A. Churchill, 1888, pp. 80.
Dobson, J. F. and Moir, P. J.: Vesico-intestinal fistula. Brit. J. Urol., **4**: 122, 1932.
Higgins, C. C.: Vesico-intestinal fistula. J. Urol., **36**: 694, 706, 1936.
Kellogg, W. A.: Vesico-intestinal fistula. Am. J. Surg., **41**: 135–186, 1938.
Rusche, C. F. and Bacon, S. K.: Vesico-intestinal fistula. Urol. & Cutan. Rev., **44**: 209, 1940.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

RECTO-URETHRAL FISTULA: REPORT OF A SUCCESSFUL REPAIR BY EXPOSURE OF THE FISTULA INSIDE THE EXTERNAL RECTAL SPHINCTER AND WITHOUT A PRELIMINARY COLOSTOMY[1,2]

LEROY J. KLEINSASSER, RALPH SMITH AND OTTO GRIFFIN
From the Departments of Surgery and Urology, Veterans Administration Hospital, Dallas, Texas

Attesting to the frequent failure of the repair of rectourethral and rectovesical fistulas, many methods for the cure of this condition have been proposed. Although any method of repair must stand the test of time, the following case merits reporting. The main features of the repair are the ease of approach to the fistula by a method described by Belt for radical perineal prostatectomy, and the use of an antibiotic, streptomycin, in place of a preliminary colostomy for fecal stream diversion from the operative site.

CASE REPORT

C. L. R., a white man, aged 23, entered the Veterans Administration Hospital, Dallas, complaining of the passage of gas through the urethra and urine through the rectum. He had been wounded by shrapnel 2 years previously, with injury to his pelvis, bladder, and rectum. He had been operated upon twice, and several perforations of the bladder were closed and a cystostomy done. Apparently no attempt was made to close the rectal perforation which he had as a result of the injury. Following this, he first noticed gas passing through his urethra, and after getting up, he noticed urine coming from his rectum. During coitus he failed to expel any semen through the urethra.

The perineum presented no unusual findings. The anal sphincter exhibited good tone. There was evidence of much scarring in the anterior rectal wall. Proctoscopic examination disclosed the patulous orifice of a fistula which entered the lower rectum, anteriorly, 5 cm. above the anal verge and from which clear straw colored fluid could be expressed. The tract seemed to extend through the prostate and seminal vesicle region. A probe could be introduced easily. A No. 21 panendoscope was passed into the bladder on July 22, 1947, and no unusual fidings were noted in the bladder or trigone. The internal vesical sphincter appeared normal. Immediately distal to the internal vesical sphincter, there was a depression on the floor, slightly to the right side, extending back to the verumontanum which was covered with mucous membrane slightly lighter in color than usual. A cystogram did not provide any unusual findings. The

---

[1] Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

[2] [illegible] nce has been presented in the literature that streptomy-
[illegible] or three days after which escape from its control of bac-
[illegible] Sulfathaladine and sulfasuxidine appear more effective for prolonged control of bacterial flora in the gastro-intestinal tract.

patient obviously had a rectourethral fistula proximal to the internal rectal sphincter.

It was elected to do a repair of the fistula without preliminary colostomy after giving him streptomycin and vitamin K orally. One gram of streptomycin was given daily. After several days of preparation the operation was performed under continuous spinal anesthesia (July 24, 1947). A suprapubic cystotomy was done through the previous suprapubic incision to divert the urine from the site of repair of the fistula. A No. 24 retention angle tube was inserted in the bladder, and the wound was closed with fine cotton sutures. The patient was then placed in an exaggerated lithotomy position and the perineum prepared with ether and tincture of merthiolate. Exposure of the recto-urethral fistula was done by the perineal approach described by Belt for radical perineal prostatectomy. A semilunar incision was made anterior to the anus, and a rubber dam was attached with Michel clips to the posterior edge of the incision to exclude the anus from the operative field. The median raphe fibers were cut. The external rectal sphincter was pushed upward and retracted anteriorly. This disclosed a thin walled rectum with absence of muscle fibers anteriorly. The mucosa of the rectum was adherent to the urethra with no interposing tissues. After placing a sound in the urethra, this was easily separated. The rectal and urethral openings were sutured with interrupted sutures of fine catgut. The muscular wall of the rectum was then repaired with interrupted sutures of fine catgut. The levator ani muscles were identified and interposed between the closed orifices of the fistula by approximation with interrupted sutures of No. 0 chromic catgut. A small rubber dam drain was inserted in the wound and the skin edges sutured with interrupted dermalon. A rubber dam drain was inserted in the rectum.

Postoperatively, streptomycin, 1 gm. daily, was given orally, and he was given 50,000 units of penicillin intramuscularly every 3 hours. He was also given tincture of opium, minims 10, to prevent bowel movements. His temperature rose to 101 F. the second day postoperatively but fell to normal the third day. The drain was removed the second day postoperatively. All sutures were removed the seventh day postoperatively from the suprapubic as well as the perineal wounds. By the twelfth day postoperatively he was having bowel movements. Eighteen days postoperatively a cystogram resulted in a left epididymitis which soon subsided. The suprapubic tube was removed and he was able to void without difficulty. He has now been observed 6 months postoperatively and has had complete recovery except for failure of ejaculation.

COMMENTS

A successful repair of recto-urethral fistula is reported without the use of preliminary colostomy but by use of streptomycin orally and by a much simplified approach described by Belt.

REFERENCES

BELT, E.: Radical perineal prostatectomy in early carcinoma of the prostate. J. Urol., 48: 287–97, 1942.

Davis, E. G.: The Young-Stone operation for urethrorectal fistula: Report of three cases. Surg., Gynec. & Obst., 32: 225–31, 1921.
Gaston, C. D. and Lee, A. B.: Recto-urethral fistula: An operation for its cure. Am. J. Digestive Diseases and Nutrition, 2: 744–6, 1936.
Lewis, L. G.: Repai [illegible] -81, 1947.
Rusche, C. F. and B [illegible]erineal prostatectomy: Report of four ca [illegible]
Tedenat: Montpelier Medicine, 16: 81–114, 1903.
Wilhelm, S. F.: Recto-urinary fistula. Surg., Gynec. & Obst., 79: 427–33, 1944.
Young, H. H. and Stone, H. B.: An operation for urethro-rectal fistula: Report of three cases. Trans. of the Am. Soc. of Genito-Urin. Surg., 8: 270–8, 1913.
Young, H. H. and Stone, H. B.: The operative treatment of urethrorectal fistula. Presentation of a method of radical cure. J. Urol., 1: 289–303, 1917.
Zimbicki: Congres Français de Chirurgie, 4: 295, 1899.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

MORPHOLOGY OF HUMAN SPERMATOZOA: OBSERVATIONS WITH THE ELECTRON MICROSCOPE[1]

ORMOND S. CULP AND JOHN W. BEST
With the technical assistance of Edna G. Jackson and Helen L. Woods
From the Division of Urology and Department of Laboratories, Henry Ford Hospital, Detroit, Michigan

Electron microscopy offers magnifications 50 times the maximum that can be obtained with the conventional light microscope. It is now possible to observe and photograph structural details too small to be seen by any other means. We have used the electron microscope to study human spermatozoa in the hope of finding some new clue that might help solve the perplexing and apparently increasing problem of male infertility. After viewing thousands of spermatozoa and studying more than 400 electron micrographs, with magnifications as great as 100,000 times, we are still unable to explain all infertility on a purely anatomic basis; but during these observations, certain morphologic details of human sperm were noted which have never been reported.

THE ELECTRON MICROSCOPE

It is important to realize that the electron microscope differs from the light microscope in several ways (table 1). It is a formidable instrument, activated by 50,000 volts, in which the illumination of the light microscope has been replaced by a stream of electrons generated by a heated wire filament (fig. 1). The path of these electrons is controlled by magnetic fields which cannot be shaped as accurately as the glass lenses of the light microscope (fig. 2).

The electron rays pass through the specimen and are affected in varying degree by its composition (fig. 3). The specimen must be much thinner than the usual histologic section and must be studied in a vacuum. Biological materials require special preparation and drying during which distortion and fragmentation should be avoided.

Electrons are invisible. Therefore, a fluorescent screen is interposed to produce a visible image of the variations in density of the specimen. Staining methods that might accentuate these differences remain in the experimental stage. Color methods are not yet available. Photographs are made by allowing the electron beam to fall directly on a photographic plate. These pictures are called electron micrographs and constitute most of the illustrations that follow.

LITERATURE

Although there have been a number of reports on electron microscopy of sperm in lower animals, very little has appeared in the literature regarding similar studies of human spermatozoa.

In 1941, Seymour and Benmosche published a brief description. They decided

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 20, 1948.

that the body was segmented instead of spiral, described a crater in the head which they interpreted as a suction cup and claimed that the tail broke up into a nondescript smudge

TABLE 1 *Differences between the light microscope and a typical magnetic electron microscope**

	LIGHT MICROSCOPE	MAGNETIC ELECTRON MICROSCOPE
Image forming radiation	Light	Electrons
Medium of travel	Air	Vacuum ($\sim 10^{-4}$ mm Hg)
Nature of lenses	Glass	Magnetic fields
Object mounting	*Glass slides*	*Thin films* ($\sim 10^{-6}$ *cm*)
Main source of contrast	Absorption	Scattering
Focusing	Mechanical	Electrical (changing objective coil current)
Adjusting magnification	Exchanging lenses	Changing projector coil current

* From Zworykin et al , Electron Optics and the Electron Microscope, John Wiley and Sons, publishers

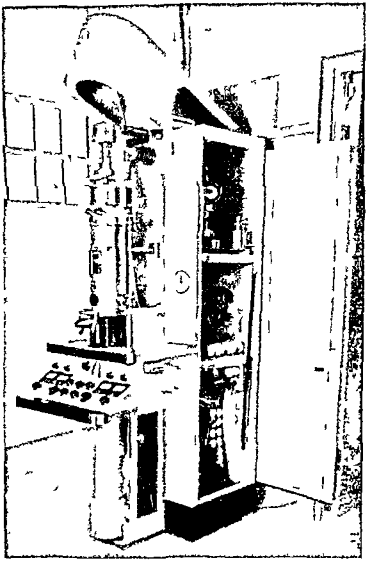


FIG 1 Type EMU, RCA electron microscope used throughout this study. (Photograph by courtesy Radio Corporation of America)

Baylor, Nalbandov and Clark, in 1943, reported that, while their studies on human semen were unsatisfactory due to the heavy accessory secretions, they were unable to find anything resembling a suction disc on the head or joints in the mid portion of the sperm, as described by Seymour and Benmosche They

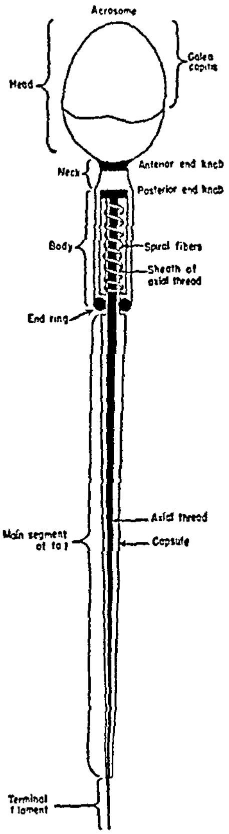


FIG. 4. Diagram of human spermatozoon as seen with light microscope (From Hotchkiss: Fertility in Men. Philadelphia: J. B. Lippincott Co., 1944.)

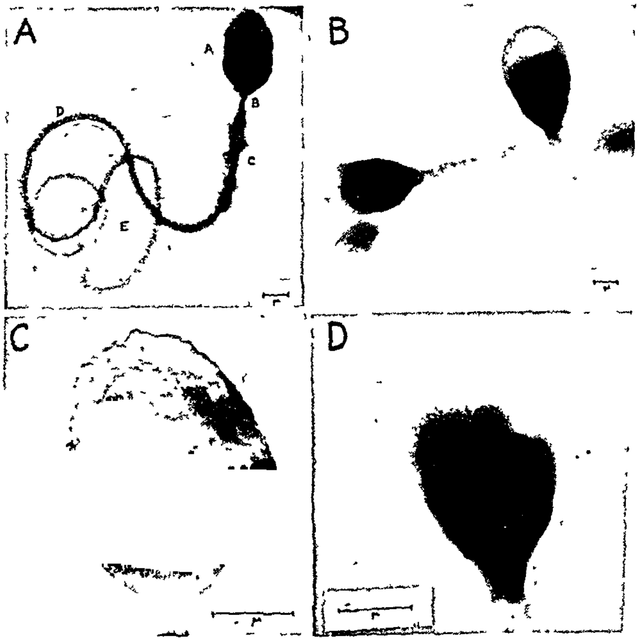


FIG. 5. *A*, upper left, sperm heads with a lighter zone at tip; A, head; B, neck; C, body; D, tail; E, terminal fibrils of tail. *B*, upper right, Shadow-cast electron micrograph of normal spermatozoon. *C*, lower left, dark-field illumination showing less dense tip of the tail. *D*, lower right, higher magnification of head with less dense tip.

illumination (fig. 5, *C*). Oil immersion study of living sperm, shadow casting with the electron microscope, and stereoscopic studies showed that the tip of the head is flattened. This difference in the appearance of the tip is probably only variation in the thickness.

Many heads contained round or ovoid areas of decreased density, as shown in figures 5, *A* and *C*. These varied in size and number and may have been vacuoles produced by preparation or by the vacuum, rather than true structural details.

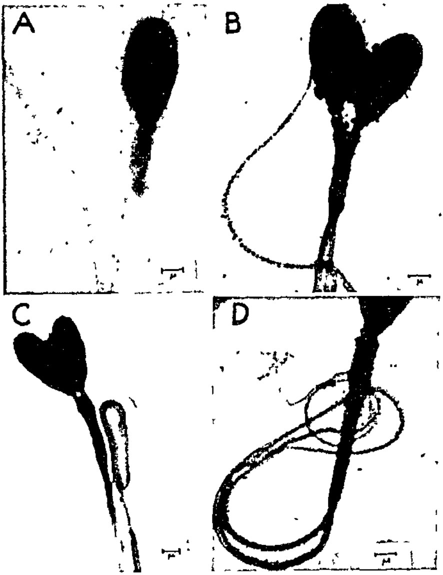


FIG. 6. *A*, upper left, membrane surrounding head, neck and body. *B*, upper right, Two spermatozoa that simulated a double head under lower magnification *C*, lower left, single spermatozoon with a double head. *D*, lower right, duplication of tail.

While a protoplasmic membrane seemed to envelop the heads of fertile bovine sperm, no similar structure has been reported in human specimens. Figure 6, *A* illustrates a typical membrane of this type. We found this only in isolated instances. The majority of the heads had no suggestion of this protoplasmic cap.

The most conspicuous feature of the heads was variation in size and shape. We are convinced that any of the grotesque forms which have been reported can be found eventually with the electron microscope. Figure 7 illustrates the most common abnormal shapes which we encountered.

Double heads proved to be rare in our experience. On many occasions we anticipated double heads with the light microscope only to find with the high

FIG. 7. Abnormally shaped heads

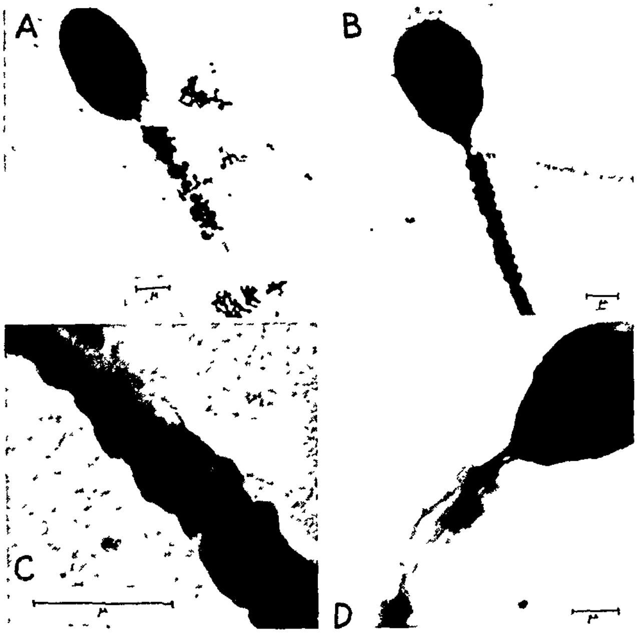


FIG. 8. *A*, upper left, partial destruction of neck and body with delicate fibers extending from head to body. *B*, upper right, typical normal body suggesting spiral loops. *C*, lower left, higher magnification of body. *D*, lower right, Fibers in neck and body, visible after disintegration of outer layers.

magnification that they were in reality 2 spermatozoa instead of partial duplication (fig. 6, *B*). True duplication of the head may occur, however, as shown in figure 6, *C*. Even double tails may be found (fig. 6, *D*).

We saw nothing suggestive of the suction cup described by Seymour and Benmosche.

As yet we have been unable to penetrate the head for study of the internal structures. It was resistant to soda bicarbonate, trypsin, papain, phenol, sodium hydroxide, chlorox, and hydrochloric acid in concentrations which did not completely destroy the organism. The coverings of the neck, body, and tail, however, could be removed with weak bases and centrifuging.

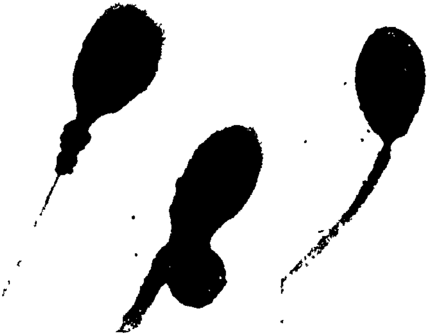


FIG. 9. Abnormal types of body

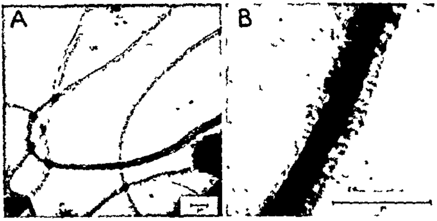


FIG. 10. *A*, left, several long narrow tails *B*, right, higher magnification of tail, showing sheath and a denser core

Neck. Most of the necks were only 0.3 μ in length. The surface sometimes had a spiral contour. When the outer covering was removed, delicate fibers of varying number were found to arise in the head and extend through the neck to the body, as shown in figures 8, *A* and *D*.

Body. This portion appeared very dense, averaged 4 μ in length and 0.7 μ in width, and presented an irregular outer margin as shown in figures 8, *B* and *C*. We think this appearance is entirely compatible with a spiral structure consisting of 10 to 15 loops.

Figure 8, *A* shows partial solution of the outer coat. Large granules formed during the disintegration. When sufficient sheath had been destroyed, clearly defined fibers were found extending the length of the body (fig. 8, *D*). These varied in number and were continuous with those in the neck.

All spermatozoa did not present well developed and sharply outlined bodies. Figure 9 illustrates some of the less distinct forms which were thought to be abnormal and just as significant as the contour of the head in identifying abnormal types.

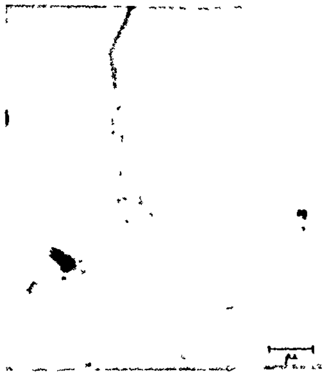


FIG. 11. Fibers in tail core after solution of sheath

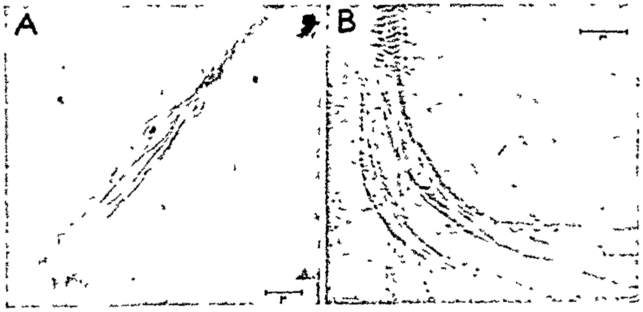


FIG. 12. *A*, left, end of tail, showing spiral structure of tail sheath and delicate terminal fibrils extending beyond sheath. *B*, right, higher magnification of end of tail sheath and projecting terminal fibrils.

Tail. Normal tails averaged 37 μ in length and 0.4 μ in width. As shown in figure 10, *A* and *B*, they seemed to consist of a sheath and a denser core. When the sheath was destroyed, discrete fibers were found running the full length of the tail (fig. 11). These were continuous with the fibers in the body.

The outer covering of the tail also had a spiral arrangement as shown in figure 12, *A*. Projecting from this sheath were numerous small fibrils (figure 12, *A* and *B*). These terminal fibrils usually numbered 10 to 12, varied greatly in length and were a consistent finding in both treated and fresh semen.

While it is possible that the fibers which extended from the head through the neck, body and tail may divide as they leave the sheath, it seems more probable that the terminal fibrils are separate units throughout the length of the spermatozoon, and that some of the delicate fibers within the tail, body, and neck are distorted or destroyed when the sheath is dissolved. These terminal fibrils probably are organs of locomotion, but they could not be seen with the light microscope and, therefore, could not be studied in fresh specimens.

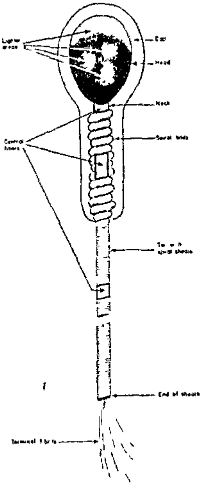


Fig. 13. Diagrammatic reconstruction of normal human spermatozoon as seen with electron microscope

SUMMARY

Our observations with the electron microscope have been summarized diagrammatically in figure 13. The normal head is ovoid, flattened at the tip, occasionally surrounded by a protoplasmic cap or envelope, and frequently contains less dense areas which may be only artifacts. Extending from the head through a short neck, spiral body, and long narrow tail are discrete delicate fibers which emerge from the sheath at the tip of the tail as 10 to 12 fine terminal fibrils.

Variations from normal have been observed in each of the 4 main anatomic divisions of the spermatozoon.

Refinements in the technique of electron microscopy should provide more complete information about sperm structure, but we believe that morphologic data will have to be correlated with the unexplored physiology of the respective parts before one can explain why some spermatozoa are incapable of fertilizing ova.

We are especially indebted to Drs. Milton E. Klinger and Edward E. Beynon of the urologic staff for routine analyses of the semen specimens; to Dr. John H. L. Watson, physicist at the Henry Ford Hospital, for his technical advice; and to Dr. Frank W. Hartman, director of laboratories, for his valuable criticisms and suggestions throughout this study.

REFERENCES

Baylor, M. R. B., Nalbandov, A. and Clark, G. L.: Electron microscope study of sperm. Soc. Exp. Biol. and Med. Proceed., **54**: 229, 1943.
Hotchkiss, R. S.: Fertility in Men. Philadelphia: J. B. Lippincott Co., 1944, p. 117.
Reed, C. I. and Reed, B. P.: Comparative study of human and bovine sperm by electron microscopy, Anat. Rec., **100**: 1, 1948.
Schmitt, F. O., Hall, C. E. and Jakus, M. A.: The ultrastructure of protoplasmic fibrils, Biological Symposia, **10**: 271, 1943.
Seymour, F. I. and Benmosche, M.: Magnification of spermatozoa by means of the electron microscope. J. A. M. A., **116**: 2489, 1941.
Zworykin, V. K., Morton, G. A., Ramberg, E. G., Hillier, J. and Vance, A. W.: Electron Optics and the Electron Microscope. New York: John Wiley and Sons, Inc., 1945, p. 88.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

DISCUSSION

DR. ROBERT S. HOTCHKISS (New York, N. Y.): The demonstrations of the internal structure of the human spermatozoa by Drs. Culp and Best are both praiseworthy and significant. Their micro-anatomical studies reveal elements in the nonnuclear portions of the cell that escape detection by other means. The numerous small fibrils in the tail segment illustrate the fact that the propulsive mechanism is far more complicated than the light microscope would indicate. Their studies imply that the point of origin of the motor impulses controlling the movement of the tail is in the caudal area of the head, for the fibers extend through the body and neck. Defective motility may eventually be correlated with structural abnormalities, an observation which would be of first rate importance.

The electron microscope has not yet afforded new revelations about the internal structure of the head of the spermatozoon. Refined techniques may resolve the problems, thereby exposing nuclear structures to this type of electronic dissection.

If patterns for nuclear composition are eventually discovered for the so-called normal ovoid head, the investigation of the misshapen or abnormal forms will be a logical sequence. This may lead to profitable information about what type of nuclear material is deposited in the ovum should fertilization occur. Furthermore, one may be able to recognize nuclear disturbances induced by harmful agents such as atomic irradiation.

It is to be hoped that the authors will pursue their interest and extend their work so well conducted thus far.

DR. HENRY K. SANGREE (Philadelphia, Pa.): Dr. Culp is to be congratulated on his excellent presentation and his prize-winning exhibit. The study of abnormal forms of sperm is one of the intriguing subjects of investigation by men interested in the study of human spermatozoa. Retzius made some excellent drawings of human sperm in 1881, and Dr. Hotchkiss was one of the first to classify the abnormal forms of human spermatozoa into some method of grouping.

The electron microscope gives us an entirely new concept of the picture of a normal sperm.

I am very much interested to know that they have not been able to show the crater or suction cap in the sperm head described by Seymour. I quote from Dr. Anderson: "It is possible that this may have been an artifact, as the technical difficulties with this instrument are very great."

Dr. Culp has also shown the tail filament to be composed of multiple fibrils, as many as eleven, changing our previous concept of the tail as a single filament; also the segmentations of the body of the sperm have now been photographed.

Perhaps the question one of my students asked me: "Does the abnormal sperm cause the embryonal malformations?" will be answered by these studies. We believe this will open up a new field for the study of the functions of the various components of the sperm.

What part do the endocrine glands play in the production of abnormal sperm? We consider that 10 per cent of abnormal sperm is within normal limits.

In a study of 222 infertile men, abnormal sperm were noted in a proportion of 20 to 50 per cent. In 222 men hypothyroidism was present in 36 men, and hyperthyroidism occurred in 24 men.

We again wish to congratulate Dr. Culp and his associates on the splendid presentation of this excellent research problem and believe he is correct in stating that the morphologic data accumulated through the study of sperm structure will aid in the solution of many cases of male infertility.

Dr. Ormond S. Culp (Detroit, Mich.): I want to thank Dr. Hotchkiss and Dr. Sangree for having discussed this paper. I can assure you that we are impressed by the fact that we have only scratched the surface and don't know if we ever will get any deeper. I hope that other urologists will become interested in this type of microscopic study.

The Journal of Urology
Vol. 61, No. 2, February 1949
Printed in U.S.A.

SOME ANTIBACTERIAL PROPERTIES OF MANDELAMINE (METHENAMINE MANDELATE)

JOHN V. SCUDI AND CHARLES J. DUCA
From the Research Laboratories of the Nepera Chemical Co., Inc. Nepera Park, Yonkers 2, New York

In a preliminary communication[1], it was reported that mandelamine is active against bacteria which cause infections of the urinary tract. It was further reported that resistance to mandelamine developed slowly, if at all, and that organisms rendered resistant to sulfathiazole or to streptomycin remained susceptible to mandelamine. This work requires extension and confirmation because important urological inferences may be drawn from the findings. Details of additional work are, therefore, set forth in the experimental part.

EXPERIMENTAL

The medium used throughout this work consisted of normal, male urine adjusted to pH 5.5 or 6.5 with phthalate or phosphate buffers in .03 and .06 molar concentration, respectively. The pH was determined before and after incubation by means of a Coleman model 3 pH electrometer. The inoculum was always 0.1 ml. of a 1:5000 dilution of an 18 hr. broth culture. Suitable control tubes of buffered and unbuffered nutrient broth and of buffered urine were included in each test. If any of the control tubes showed no growth, the entire series of tubes was discarded. Eight stock laboratory strains of bacteria commonly found in urinary tract infections were studied at pH 5.5 and 9 strains of organisms recently isolated from urinary tract infections were studied at both pH 5.5 and 6.5. Minimal bacteriostatic concentrations of mandelamine, sulfathiazole, and streptomycin were determined by means of a serial two-fold dilution method. End-points were taken as the lowest drug concentrations at which no growth occurred after 72 hours incubation. Bactericidal activity was determined by subculturing 0.25 ml. of each apparently negative tube into 5 ml. of nutrient broth followed after 72 hours of incubation by examination for visible growth. All tests were repeated at least 5 times, and the figures given in the tables represent the averages of these 5 tests.

Attempts were made to induce resistance to the substances under test. Three strains of bacteria were used with sulfathiazole, 3 with streptomycin, and all 6 against mandelamine. One-tenth ml. of an 18 hour nutrient broth culture was inoculated into 5 ml. of sterile urine, buffered at pH 5.5, in the presence of serial two-fold dilutions of the individual drugs. After 72 hours' incubation, 0.1 ml. samples were taken from the tubes containing the highest drug concentrations in which growth had occurred. These were transferred into tubes containing a higher series of drug concentrations, and so on. When organisms developed resistance to sulfathiazole and streptomycin they were inoculated into sterile nutrient broth, pH 7.1, in order to permit solution of higher concentrations of sulfathiazole and to test streptomycin in a more favorable environment. Finally, the susceptibility of sulfathiazole and streptomycin resistant organisms to mandelamine was determined.

---

[1] Duca, C. J. and Scudi, J. V.: Proc. Soc. Exp. Biol. & Med., 66: 123–126, 1947.

It will be noted that the inoculum used in the resistance studies was 5000 times that used in determining antibacterial activity. Since the size of the inoculum is of critical importance in determining the antibacterial activity of sulfonamides[2] and of streptomycin[3], the effect of inoculum size on the rate of development of resistance to the different drugs was studied in a third experiment. The procedure was identical to that of experiment 2, with the one exception that the inoculum was 0.5 ml.

Finally, because we are presently concerned with the testing of tuberculostatic compounds, mandelamine was tested against M. tuberculosis hominis H37 RV and M. tuberculosis bovis B1. A 10 day old culture of the tubercle bacilli in Dubos' medium[4] was diluted so that 60 per cent transmission of light was obtained in a Lumetron colorimeter. One-tenth ml. of this dilution was then inoculated into 6.1 ml. of Dubos' medium (pH 6.5) in the presence of serial two-fold dilutions of mandelamine. Results were read after 10 days' incubation and the presence of acid fast bacilli was verified by Ziehl-Neelsen stains of smears. This test was repeated on 6 different occasions.

TABLE 1. *Stock laboratory strains in normal sterile urine buffered at pH 5.5. Minimal bacteriostatic and bactericidal concentrations of mandelamine, streptomycin and sulfathiazole given in mg. per cent. Each figure is the average of 5 different series of tests.*

	MANDELAMINE		STREPTOMYCIN		SULFATHIAZOLE	
	static	cidal	static	cidal	static	cidal
E. coli 64	50	50	20	20	5	10
E. coli 4R5190	50	50	20	20	7.5	20
A. aerogenes 129	25	25	20	20	3	5
K. friedlanderi type A F12	12.5	12.5	5	5	5	10
K. friedlanderi type B EGS	25	25	5	5	5	10
St. aureus 209	15	25	10	20	2.5	10
St. aureus SM	20	25	40	40	10	10
Ps. aeruginosa ATCC 9029	40	40	40	40	6.25	20

Results. The average minimal bacteriostatic and bactericidal concentrations of sulfathiazole, streptomycin, and mandelamine at pH 5.5 against the 8 stock laboratory strains are shown in table 1. The results indicate that minor differences in potency exist, but, in general, the activity of all 3 drugs is of the same order of magnitude.

The data obtained at pH 5.5 and 6.5 with the 9 strains recently isolated from urinary tract infections are shown in table 2. The results indicate that streptomycin is somewhat less active at pH 5.5 than at 6.5. This observation is in accord with earlier work. Although solutions of streptomycin kept at a low pH for 24 hours regain their original activity at pH 7.8[5], the decreased activity of streptomycin with decreasing pH is well known[6]. Sulfathiazole is about equally active at both pH levels but the threat of sulfonamide urolithiasis[7] at the lower level should preclude its use in acidic urine. Mandelamine is definitely more effective at the lower pH, but at either pH level bactericidal concentrations are low enough to permit ready attainment in the urine by appropriate dosing.

---

[2] Henry, R. J.: The mode of action of sulfonamides. Josiah Macy, Jr. Foundation, Review Series, 2: 151, 1944.

[3] Lenert, T. F. and Hobby, G. L.: Proc. Soc. Exp. Biol. & Med., 65: 235–242, 1947.

[4] Dubos, R. J. and Davis, B. D.: J. Exp. Med., 83: 409–423, 1946.

The pH changes produced by the organisms in the absence of the drugs, and in the presence of ineffective amounts of the drugs, are recorded in tables 3 and 4. The results indicate that in spite of the buffer systems employed, the pH was strikingly increased when 3 of the organisms were allowed to grow in the absence of adequate concentrations of the antibacterial agents. These organisms, St. aureus 209, A. aerogenes Harrington, St. albus No. 6 are of particular interest and will be discussed later. It is important here to emphasize the fact that in the presence of adequate concentrations of the drug these same organisms produced no significant change in pH.

TABLE 2. *Recently isolated strains in normal sterile urine buffered at pH 5.5 and 6.5. Minimal bacteriostatic and bactericidal concentrations given in mg. per cent. Each figure is the average of 5 different series of tests.*

	MANDELAMINE				STREPTOMYCIN				SULFATHIAZOLE			
	5.5		6.5		5.5		6.5		5.5		6.5	
	static	cidal	static	cidal	static	cidal	static	cidal	static	cidal	static	cidal
E. coli Grogan	25	25	62.5	62.5	10	15	5	10	1.56	5	1.25	20
E. coli Fernande	50	50	150	150	15	15	5	10	10	20	0.6	0.6
E. coli Travis	50	50	125	125	20	20	5	5	3	10	1.25	40
A. aerogenes Harrington	30	30	62.5	62.5	3	5	2.5	2.5	20	20	2.5	40
St. albus No.6	25	50	75	75	20	20	10	15	0.625	2.5	1.25	20
St. albus Agostini	125		75	75	40		10	20	5		1.25	5
St. hem. No. 9	62.5		50	50	20		20	20	2.5		0.6	0.6
Ps. pyocyaneus No.7	125	125	200	200	40	40	20	30	5	40	20	40
Ps. aeruginosa Fox	62.5	62.5	200	200	20	20	5	10	2.5	10	2.5	20

The results of the resistance studies are presented in tables 5 and 6. It is readily apparent, from table 5, that the organisms rapidly developed resistance to sulfathiazole and streptomycin and in the latter case to an extraordinary degree. The degree of resistance to these drugs can undoubtedly be further increased under the proper conditions, but in the present work 75 mg. per cent of sulfathiazole was accepted as a limit because this represents the concentration of a saturated solution at pH 5.5. The 1000 mg. per cent concentration of streptomycin was taken as a convenient point at which to stop, though with St. aureus SM resistance to streptomycin developed so quickly that within 8 transfers the organism grew in 2000 mg. per cent of the drug. When the resistant organisms were transferred to sterile nutrient broth at 7.1, they grew in the presence of 100 mg. per cent sulfathiazole and in 1500 mg. per cent streptomycin or more, respectively. In striking contrast with the foregoing, none of the organisms developed resistance to mandelamine, even after 10 transfers. Further, with this drug bacteriostatic and bactericidal concentrations remained equal to each other. After the organisms had developed resistance to sulfathiazole or streptomycin they were challenged with serial two-fold dilutions of mandelamine in urine at pH 5.5. No significant change in the susceptibility of the resistant organisms to mandelamine was observed. Thus, it would appear that resistance to mandelamine is developed very slowly if at all, and that sulfathiazole-resistant or streptomycin-resistant organisms retain their full susceptibility to mandelamine.

---

[5] Berkman, S., Henry, R. J. and Housewright, R. D.: J. Bact., 53: 567–574, 1947.
[6] Wolinsky, E. and Steenken, W.: Proc. Soc. Exp. Biol. & Med., 62: 162–165, 1946.
[7] Scudi, J. V.: Am. J. Med. Sc., 211: 615–628, 1946.

TABLE 3. *pH after 72 hrs. incubation in normal sterile urine buffered at pH 5.5, in the presence of ineffective amounts of drugs*

	WITHOUT DRUG	MANDELAMINE	STREPTOMYCIN	SULFATHIAZOLE
E. coli 64	5.6	5.7	5.6	5.6
E. coli 4R5190	5.7	5.9	5.6	5.6
A. aerogenes 129	7.2	5.6	5.6	5.6
K. friedlanderi Type A F12	6.3	5.9	5.7	5.9
K. friedlanderi Type B EGS	6.2	5.8	5.8	5.9
St. aureus 209	8.5	8.5	8.6	8.6
St. aureus SM	5.7	5.5	5.6	5.5
Ps. aeruginosa ATCC 9029	6.7	6.6	6.6	6.6

TABLE 4. *pH after 72 hrs. incubation in normal sterile urine buffered at pH 6.5, in the presence of ineffective amounts of drugs*

	WITHOUT DRUG	MANDELAMINE	STREPTOMYCIN	SULFATHIAZOLE
E. coli Grogan	6.8	6.8	6.8	6.7
E. coli Fernande	6.7	6.6	6.6	6.6
E. coli Travis	6.8	6.7	6.8	6.7
A. aerogenes Harrington	8.3	7.0	8.2	7.9
St. albus No. 6	8.4	7.7	8.6	8.1
St. albus Agostini	6.6	6.9	6.6	6.6
St. Hem. No. 9	6.6	6.6	6.6	6.6
Ps. pyocyaneus No. 7	7.0	7.0	7.0	6.8
Ps. aeruginosa Fox	6.7	6.8	6.8	6.6

The results of the resistance studies with the larger inoculum are presented in table 5, but are perhaps more clearly set forth in figures 1–3. As would be anticipated because of the larger inoculum, higher concentrations of the antibacterial drugs were required to suppress growth of the first culture. This observation is in full accord with previous findings on virtually every antibacterial agent studied. Much more important is the observation, delineated in the chart, that resistance appeared to develop more rapidly with the larger inoculum. The implications of this finding, if confirmed by further detailed study, would be of great theoretical and practical interest. The charts also show the rapid rate of increase in resistance to sulfathiazole and to streptomycin in contrast with the erratic seesaw results obtained with mandelamine. It is important to note that the upper limits of sulfathiazole and streptomycin were imposed by solubility in the one case and by convenience in the other. No such

TABLE 5. *Induced resistance to sulfathiazole, streptomycin and mandelamine. Minimal bacteriostatic concentrations of mandelamine before and after development of resistance to sulfathiazole and to streptomycin. Concentrations given in mg. per cent. Inoculum 0.1 ml. Each figure is the average of 2 different series of tests.*

ORGANISM	SULFATHIAZOLE			STREPTOMYCIN			MANDELAMINE					
	E coli G	Aero aero H	S aur 209	E coli 64	Aero aero 129	S aur SM	E coli G	Aero aero H	S aur 209	E coli 64	Aero aero 129	S aur SM
Original minimal bacteriostatic concentration..	2.5	10	2.5	10	10	20	50	100	25	100	50	12.5
Final minimal bacteriostatic concentration	Sat	Sat	Sat	1000	1000	2000	125	125	15.6	250	125	15.6
Increase in resistance	*30*	*7.5*	*30*	*100*	*100*	*100*	*2.5*	*1.25*	*1*	*2.5*	*2.5*	*1*
Number of transfers..	6	4	6	10	8	8	10	10	10	10	10	10
Original minimal bacteriostatic concentrations of mandelamine .	50	100	25	100	50							
Minimal bacteriostatic concentration of mandelamine after induction of resistance .	62.5	62.5	62.5	250	15.6							

TABLE 6 *Induced resistance to sulfathiazole, streptomycin and mandelamine. Minimal bacteriostatic concentrations of mandelamine before and after development of resistance to sulfathiazole and to streptomycin Concentrations given in mg per cent. Inoculum 0.5 ml. Each figure is the average of 2 different series of tests*

ORGANISM	SULFATHIAZOLE			STREPTOMYCIN			MANDELAMINE					
	E coli G	Aero aero H	S aur 209	E coli 64	Aero aero 129	S aur SM	E coli G	Aero aero H	S aur 209	E coli 64	Aero aero 129	S aur SM
Original minimal bacteriostatic concentration	20	20	20	50	50	15	25	100	200	200	200	20
Final minimal bacteriostatic concentration	(ca 75 mg %) >Sat	>Sat	>Sat	1500	1200	1500	75	300	75	600	150	20
Increase in resistance	>4X	>4X	>4X	30X	24X	100X	3X	3X	−1.7X	3X		
Number of transfers	5	3	3	8	10	9	9	10	10	9	10	9
Original minimal bacteriostatic concentration of mandelamine	25	100	200	200	200	20						
Minimal bacteriostatic concentration of mandelamine after induction of resistance	75	300	500	150	75	37.5						

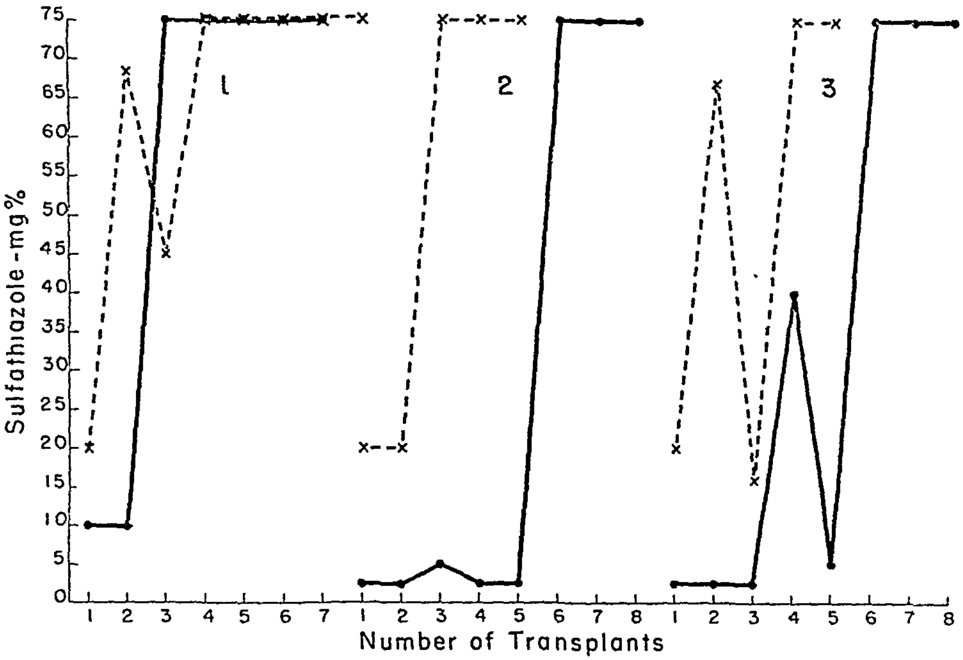


FIG. 1. Development of resistance to sulfathiazole. Transplants every 3 days. Broken line, inoculum 0.5 ml. Solid line, inoculum 0.1 ml. *1*, A. aerogenes Harrington. *2*, E. coli Grogan. *3*, S. aureus 209.

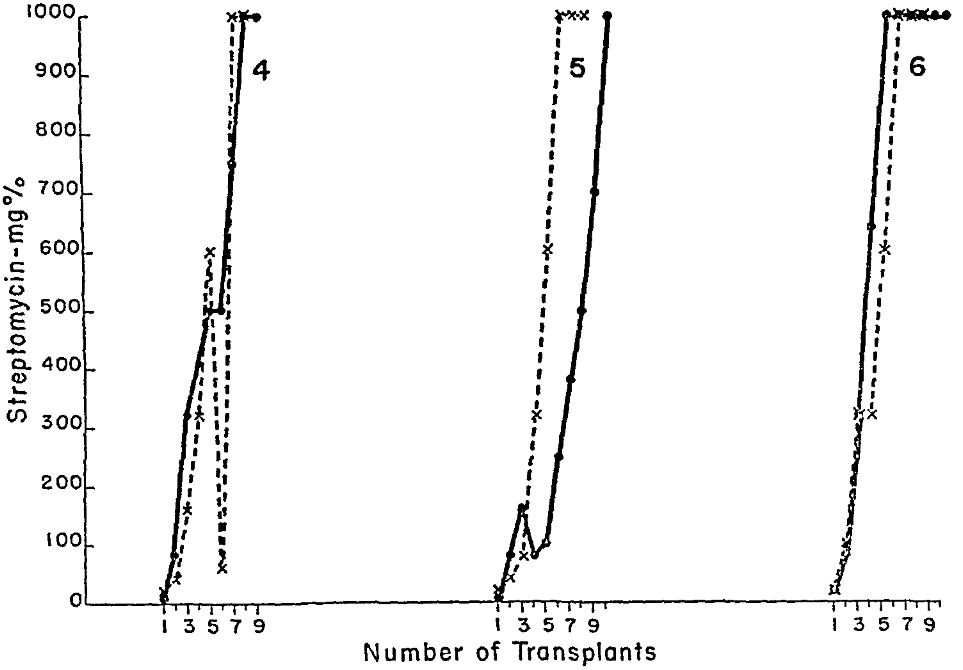


FIG. 2. Development of resistance to streptomycin. Transplants every 3 days. Broken line, inoculum 0.5 ml. Solid line, inoculum 0.1 ml. *4*, A. aerogenes 129. *5*, E. coli 64. *6*, S. aureus SM.

limitations were imposed upon mandelamine. Yet, regardless of the size of inoculum, none of the organisms developed resistance to the latter drug. The fluctuations of the curves in figure 3 fall well within the experimental error inherent in serial two fold dilution methods From these curves it would appear that almost any organism, independent of its history, would be inhibited by mandelamine at concentrations of 300 mg per cent

The results of the in vitro tests of mandelamine against tubercle bacilli showed that the drug is active against the human strain (H37RV) at 4 mg per cent and against the bovine strain (B1) at 16 mg per cent in Dubos' medium at pH 6 5 *Further in vitro and in vivo studies on this interesting finding are under investigation*

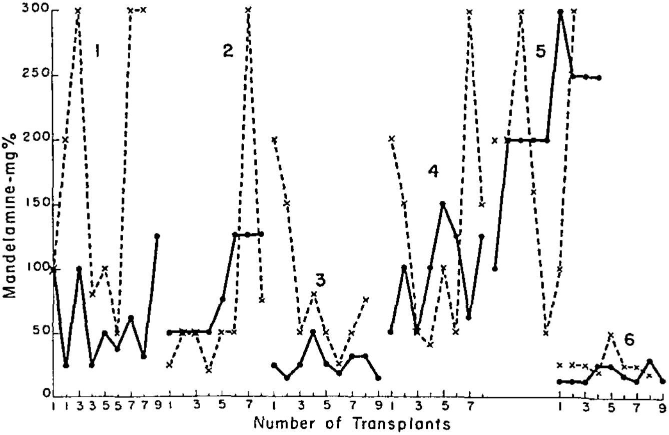


FIG 3 Nondevelopment of resistance to mandelamine Transplants every 3 days Broken line inoculum 0 5 ml Solid line, inoculum 0 1 ml *1* A aerogenes Harrington *2*, E coli Grogan *3*, S aureus 209 *4*, A aerogenes 129 *5*, E coli 64 *6* S aureus SM

Discussion The results described in the previous sections extend and emphasize the findings of our preliminary communication[1] Mandelamine is effective against bacteria which commonly invade the urinary tract, such organisms do not develop resistance to mandelamine, and organisms rendered resistant to sulfathiazole or to streptomycin remain fully susceptible to mandelamine These findings taken in conjunction with clinical reports[8] [9] lead to important urological inferences, some of which are discussed in the following paragraphs

In recent years, the successes achieved in the treatment of urinary tract infections with sulfonamide drugs have led to the abandonment of many therapeutic agents and have tended to restrict the search for new drugs Wider clinical experience with the sulfonamide drugs, however, has disclosed that they possess toxic properties and should not be administered without adequate medical supervision. The danger of toxic reactions rightfully precludes administration of the sulfonamides to patients who require protracted therapy. The same limitations must be imposed upon the use of streptomycin but with this agent the development of drug-fastness imposes the additional limitation that practically all organisms develop resistance to streptomycin with remarkable rapidity. Indeed, Hewitt[10] states that persistence of bacteria in the urine after 48 hours of streptomycin therapy usually signifies that the organisms have become resistant. He points out that the development of resistance is the major cause of failure to achieve sterilization of the urinary tract. Quite clearly, then, the protracted use of the sulfonamides and streptomycin in the treatment of urinary tract infections is not feasible.

---

[8] Carroll, G and Allen H W J Urol , **55** 674–681, 1946

[9] Kirwin, T J and Bridges, J P Am J Surg , **52** 477–480, 1941

In contrast with the sulfonamides and streptomycin, Kirwin and Bridges[8] and Carroll and Allen[9] have demonstrated that, in addition to its clinical effectiveness, mandelamine exhibits a remarkable lack of toxicity. These authors have administered mandelamine to patients over considerable periods of time with a negligible incidence of unimportant side reactions. These findings, together with the fact that organisms do not develop resistance to mandelamine, suggest that mandelamine will be the drug of choice in the treatment of patients who require prolonged therapy and repeated instrumentation. It may be desirable, in the management of patients requiring surgical procedures, to begin therapy with mandelamine preoperatively; immediately before and for 2 to 4 days after operation, the sulfonamide drugs or the antibiotics might be employed in maximum doses; and finally, mandelamine might be administered postoperatively. In this way one would anticipate maximum effectiveness, with a minimum danger of toxic reactions, and a negligible possibility of drug resistance.

The fact that mandelamine is effective in vitro against sulfathiazole and streptomycin resistant organisms strongly recommends the use of the drug in the treatment of patients suffering infections due to resistant organisms.

Approximately 10 to 20 per cent of urinary tract infections are caused by bacteria which produce such large increases in the alkalinity of the urine that they do not respond readily to simple mandelamine therapy. It would appear, as a rational approach to the therapy of these infections, that a preliminary acidification of the urine for only 24 to 36 hours would suffice to permit control of these organisms by mandelamine. This short period of acidification would not impose undue hardships, and would permit maximum antibacterial efficiency. There is, moreover, a second factor involved. Mandelamine improves its own environment by acting as an acidifying agent. This fact has been stressed by Carroll and Allen who report that "the urine of all patients (200) in the series but 8 became or remained acid on this therapeutic regimen without medication or restriction of diet or fluid intake." By the exploitation of these two properties of mandelamine, infections caused by bacteria which increase the alkalinity of the urine may more adequately be brought under control.

---

[10] Hewitt, W. L.: Am. J. Med., **2**: 474–484, 1947.

The foregoing discussion would seem to justify wider clinical use of mandelamine in the field of urological therapeutics.

SUMMARY

Comparison of mandelamine, streptomycin, and sulfathiazole against microorganisms *recently isolated from urinary tract infections indicates that their* activities are not widely different. Organisms developed resistance to sulfathiazole and streptomycin rapidly and to a remarkable degree. In contrast with these results, resistance to mandelamine did not appear at all. Organisms rendered resistant to sulfathiazole or streptomycin retained full susceptibility to mandelamine. The implications of these findings are briefly discussed.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

A NEW ANESTHETIC LUBRICANT

A. D. GORFAIN

The ideal medium for instrumentation of the genito-urinary tract should be both an efficient anesthetic and an antiseptic lubricant. Surfacaine (p-cyclohexyloxybenzoate, Lilly) in its prepared vehicle comes nearest to this. The anesthetic is the twenty-seventh in a group of 90 substituted piperidino-alkyl benzoates prepared and tested by McElvain and Carney. The first in this group is Metycaine (Lilly) whose well known general usefulness as a local anesthetic suggested the investigation of similar compounds. Its profound anesthetic characteristics and lack of toxicity have found clinical acceptance in the treatment of painful skin and rectal lesions, and prompted its trial as a topical anesthetic in urology.

Over two hundred cystoscopic examinations and treatments have been performed using Surfacaine, 0.75 per cent in a water soluble, clear jelly base by the following technique: The medium is sufficiently fluid to permit ready filling of a glass Luer syringe with a rubber acorn tip. Ten cubic centimeters with 2 cc air following are injected into the average male urethra and a Hyams's penile clamp put on; 3 to 4 cc are used in the female and retains itself. After 5 minutes the meatus is occluded by the instrument being used, the clamp removed and the instrument passed into the bladder. This keeps the anesthetic lubricant in the urethra throughout the examination with obvious benefits. Heretofore it has been usual to inject an aqueous anesthetic agent and then use a jelly lubricant on the instrument. The sterility of that squeezed out of a tube which has been used many times previously is doubtful. With the method and medium described above, this second step and its attendant likely contamination is eliminated.

There has been, without exception, complete anesthesia of the urethral mucosa without a sign of toxicity in any case. The male patients remark only of the moderate pressure concomitant with straightening of the posterior urethral curve. The small amount of medium in the bladder readily washes out. No precipitation has been noted on the mucous membranes in either acid or alkaline urines. To determine possible changes in the mucosa incident to the action of the drug, 3 patients accustomed to instrumentation without anesthesia were cystoscoped. The color, vascularity, and other characteristics of the mucosal surface were carefully noted. Cystoscopy was reported after the patients had retained the anesthetic for 10 minutes. No blanching, hyperemia, edema, or other changes were noted which might give a false impression of the mucous membranes being observed.

The drug has added advantages in its being able to withstand boiling and autoclaving to at least 115 C. The addition of a suitable agent to make it antiseptic or bactericidal is being investigated.

Addendum: Since the manuscript was submitted for publication, the addition of an agent to make the preparation antiseptic or bactericidal has been investigated by the Lilly Biological Laboratories. It has been found, by the F.D.A. germicidal tests, that all Surfacaine products are self-sterilizing, and the addition of other antiseptics is unnecessary.

SUMMARY

Surfacaine in a suitable jelly medium is a superior anesthetic lubricant for the local anesthesia and lubrication necessary to satisfactorily instrumentate the genito-urinary tract.

1033 Gayley Ave., Los Angeles 24, Calif.

REFERENCE

McElvain, S. M. and Carney, T. P.: Piperidine derivatives. XVII. Loca anesthetics derived from substituted piperidinoalcohols. J. Am. Chem. Soc., 68: 2592, 1946.

THE JOURNAL OF UROLOGY
Vol. 61, No. 2, February 1949
Printed in U.S.A.

A NEW DISPOSABLE RUBBER URINAL FOR MALES

C. ABERHART

From the Department of Surgery, Toronto General Hospital and Department of Urology, Christie Street Hospital Department of Veterans Affairs, Toronto, Ontario, Canada

Three years ago we became interested in the treatment and rehabilitation of paraplegic patients. Their disability had followed injury to the spine and spinal cord while serving in the army overseas.

By the development of a satisfactory tidal irrigator, and by the use of streptomycin and surgery, including transurethral resection, these patients arrived at a stage where they were able to empty their bladder satisfactorily without the use of tubes.

The chief problem then confronting us was some method of adequately protecting these patients from urinary accidents commonly associated with the automatic bladder and from stress incontinence which occurs during the physical exertion of crutch and brace walking. The available urinals have been utilized and are only moderately successful. The chief difficulties with the present day urinals are as follows:

The bulk of the penile portion of the apparatus renders the patient conscious of the fact that he is wearing a urine collecting apparatus.

The rubber used in the manufacture is very heavy and tends to produce marked excoriation of the skin.

There is not sufficient capacity in the penile sheath portion, in spite of its bulk, to take care of the sudden emptying of an automatic bladder, particularly in a sitting or lying position. As a result urinary accidents are not avoided and the patient becomes wet.

The tightly fitting, cumbersome, heavy rubber penile sheath tends to produce pressure sores in these paraplegic patients.

The apparatus is difficult and tedious to keep dry and clean, and for this reason more than one urinal per patient is required.

Because of these difficulties we have devised a new type of rubber urinal (fig. 1, *A*) which embodies the following principles:

It is designed so that the upper or penile portion is made in various sizes and allows accurate fitting of the individual patient. Immediately below this penile sheath is an expanded bulb-like portion which will hold the contents of an automatic bladder adequately (fig. 1, *B*).

The whole sheath is made of fine Latex rubber which prevents excoriation.

The sheaths are inexpensive and are not designed as a permanent fixture, but rather, as the part of the urinal which can be discarded and a new one applied.

The new sheath is non-bulky.

There is no ring on the upper portion of the penile sheath to produce pressure sores even if the urinal is anchored to the penis with a half circle of elastoplast.

THE JOURNAL OF UROLOGY

Manuscripts submitted for publication and communications concerning editorial matters should be sent to Dr. J. A. Campbell Colston, Brady Urological Institute, Johns Hopkins Hospital, Baltimore 5, U. S. A.

Reprints of articles will be furnished to contributors when ordered in advance. A table showing cost of reprints, with an order slip, is sent with proof.

THE JOURNAL OF UROLOGY is issued monthly. Two volumes are issued each year beginning in January and July.

Correspondence concerning business matters should be addressed to The Williams & Wilkins Company, Publishers of Scientific Books and Periodicals, Mount Royal and Guilford Avenues, Baltimore, U. S. A.

Subscription price: $5.00 per volume. For countries outside the Postal Union (North and South America and Spain), add 50 cents per volume, for delivery.

Claims for copies lost in the mails must be received within 30 days (domestic). Changes of address must be received within two weeks of the date of issue.

New subscriptions and renewals are entered to begin with the first issue of the current volume. Should any issue of the current volume be out of print at the time the subscription order is received, the pro-rata value of such numbers will be credited to the next volume, and the renewal invoice therefore adjusted accordingly.

Subscriptions should be renewed promptly—To avoid a break in your series, subscriptions should be renewed promptly. The publishers cannot guarantee to supply back issues on belated renewals.

Subscriptions, new or renewal, should be sent to the Publishers or to Agents listed below.

Vol-61 No-3, March 1949

AGENTS

For Australia: Angus & Robertson, Limited, 89–95 Castlereagh Street, Sydney.

For the British Empire, except Australia and Canada: Baillière, Tindall & Cox, 8 Henrietta St., Covent Garden, WC. 2, London, England.

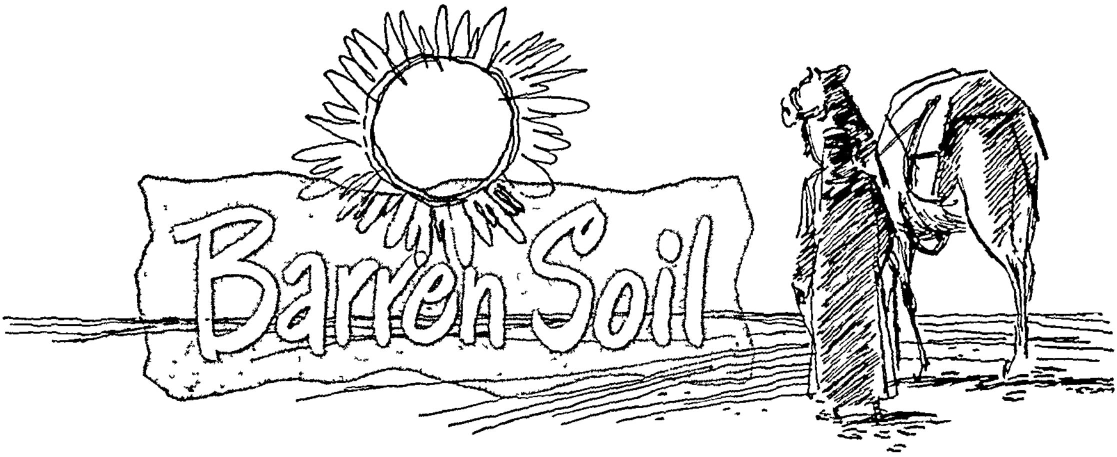
For Canada: Wm. Dawson & Sons Ltd., 70 King Street East, Toronto.

PUBLISHED MONTHLY BY

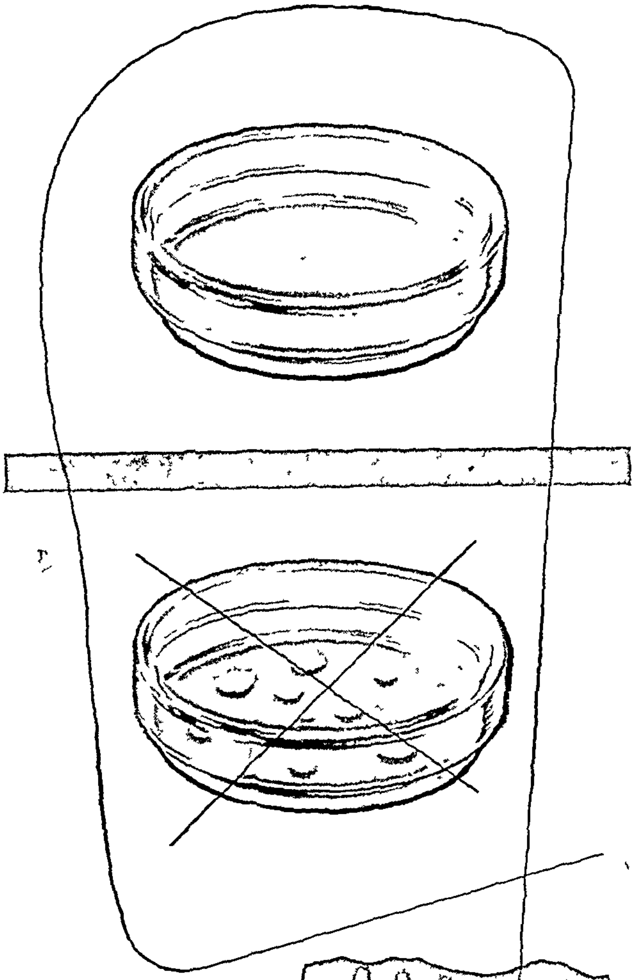
THE WILLIAMS & WILKINS COMPANY

Publishers of Scientific Books and Periodicals

BALTIMORE-2. U. S. A.



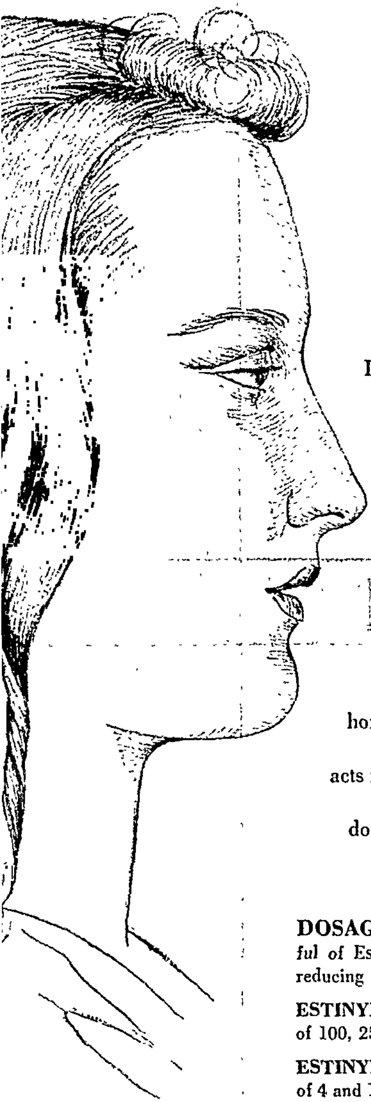
ASSURANCE OF PENICILLIN STERILITY



MICROBIAL COUNT FOR STERILITY
—one of the 138 tests made by Abbott in the production of dependable penicillin This test is made at the start, middle and end of the filling of each lot of penicillin ointment. One and one-fourth grams of ointment (2 cc) are weighed into a sterile bottle, melted and mixed with 18 cc. of water. One-half cc. of clarase, an enzyme to neutralize the effect of the penicillin, is added to the mixture. This permits any organisms in the ointment to grow out. Four cc. of the mixture (representing 0.25 Gm. of ointment) is poured into each of two petri dishes containing nutrient agar. These are incubated for 48 hours at 37° C. Then the colonies of micro-organisms in both dishes are counted and multiplied by two to give an estimate for 1 Gm. of ointment. F.D.A regulations specify that the number of viable micro-organisms in 1 Gm. of ointment must not exceed 50.

Varied and exacting tests—138 in all—are your assurance that Penicillin, Abbott, can be used *with confidence.* These 138 Abbott tests, exclusive of those conducted by the Food and Drug Administration, cover every stage of the production process. They include such factors as mold contamination, potency, sterility, pyrogens, toxicity, penicillin G content, pH, heat stability, moisture content, crystallinity and clarity. Thus you can be sure that Penicillin, Abbott, is absolutely dependable, whether supplied in vials, cartridges, tablets, troches, Dulcet® tablets or ointments. Remember the name Abbott whenever penicillin therapy is required. Prescription pharmacies everywhere carry Abbott Penicillin Products.
ABBOTT LABORATORIES, North Chicago, Ill.
®Medicated Sugar Tablets, Abbott.

SPECIFY Abbott PENICILLIN PRODUCTS



by far the most potent ORAL ESTROGEN available clinically

In exceedingly minute doses—as little as 0.02 mg. (1/3200 gr.) daily—Estinyl* maintains the average menopausal patient free of symptoms. Even when initiating therapy and in the more severe cases, unusually small dosage—measured in hundredths of a milligram—has been found effective.

ESTINYL

(ETHINYL ESTRADIOL)

Estinyl, a derivative of the ovarian follicular hormone, estradiol, evokes the sense of well-being characteristic of natural hormone therapy. It acts rapidly, often completely controlling climacteric symptoms within a few days. In therapeutic dosage side effects are notably infrequent. Unique response to minimal dosage permits effective estrogen therapy at low cost to patients.

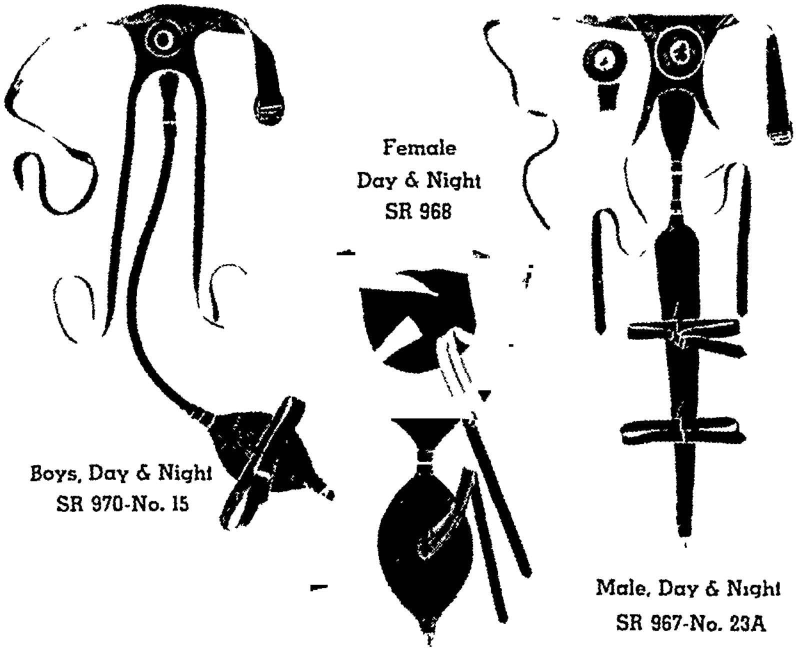
DOSAGE: One Estinyl Tablet (0.02 mg.) or one teaspoonful of *Estinyl Liquid (0.03 mg.) daily, may be prescribed,* reducing dosage as symptoms subside.

ESTINYL Tablets, 0.02 (buff) or 0.05 mg. (pink), in bottles of 100, 250 and 1000.

ESTINYL Liquid, 0.03 mg. per 4 cc. (teaspoonful), in bottles of 4 and 16 oz.

*®

Schering CORPORATION · BLOOMFIELD, NEW JERSEY
IN CANADA, SCHERING CORPORATION LIMITED, MONTREAL



SEAMLESS
HOSPITAL STANDARD
Urinals

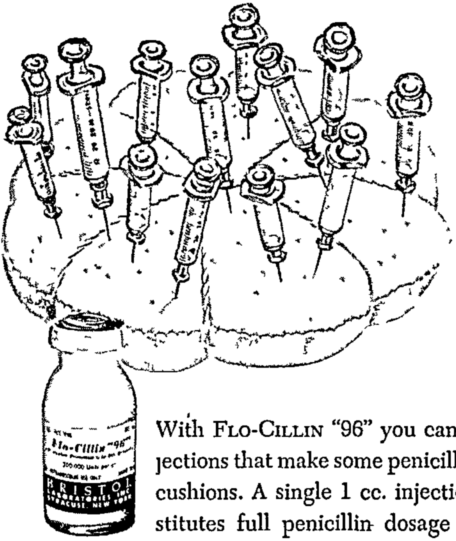
NEW STANDARDS OF CLEANLINESS AND COMFORT

Your patients will appreciate the cleanliness, comfort and safety of the new SEAMLESS Hospital Standard Urinals . . . *Completely redesigned* with basic improvements recommended by eminent G. U. specialists . . . *Handmade* from the finest materials available. Shown above are just three urinals in the most *complete* line manufactured—one for every special need. You can recommend them to your patients with assurance of outstanding quality. Write Dept. J for booklet describing the complete line. SEAMLESS Urinals are sold through leading drug stores and surgical supply houses.

REG. U. S. PAT. OFF.

FINEST QUALITY SINCE 1877

SURGICAL RUBBER DIVISION
THE SEAMLESS RUBBER COMPANY
NEW HAVEN 3, CONN., U. S. A.



With FLO-CILLIN "96" you can avoid the frequent injections that make some penicillin patients feel like pincushions. A single 1 cc. injection every 48 hours constitutes full penicillin dosage in all but exceptional cases. And this gives ample margin for safety, because this single injection of 1 cc. provides therapeutic blood levels for 96 hours in 90% of patients.

Free-flowing FLO-CILLIN "96" spares you many annoyances too. It is constantly fluid, needs no prolonged shaking, won't "settle out." Whether your syringe is wet or dry, it won't clog the needle. It saves your time in office and home treatment, and of course it saves valuable nursing time in the hospital.

You can obtain this remarkable new repository penicillin from your usual source of supply. In rubber-capped 10 cc. vials, and in 1 cc. cartridges for use with the B-D Disposable Cartridge Syringe and the B-D Metal Cartridge Syringe.

Flo-Cillin "96"

Bristol Laboratories Trademark For
CRYSTALLINE PROCAINE PENICILLIN G IN OIL
(300,000 units per cc)
WITH ALUMINUM MONOSTEARATE, 2%

Bristol
LABORATORIES INC.
SYRACUSE, NEW YORK

(In writing to advertisers, please mention the journal—it helps.)

Are you confused

when considering
which androgenic preparation to use?

Recent conflicting statements on the relative potencies and use of various testosterone* products for parenteral administration indicate—more than ever—the wisdom of using Council-Accepted androgenic preparations.

Established therapeutic claims and approved advertising copy are assured with Testosterone Propionate "Rare", the only androgenic preparation for intramuscular use which bears the seal of acceptance of the Council on Pharmacy and Chemistry of the American Medical Association.

*Popularly known as "male sex hormone".

None is more potent for intramuscular use than

TESTOSTERONE PROPIONATE *"Rare"*

Testosterone Propionate "Rare":
1 cc. ampules, 5, 10 and 25 mg.
in boxes of 3, 6 and 50;
also 10 cc. vials, 25 mg. per cc.,
and 6 cc. vials, 50 mg. per cc.

Methyl Testosterone "Rare":
Scored tablets, 10 mg. (white)
and 20 mg. (pink); bottles of
30 and 100.

Rare Chemicals, Inc. HARRISON, NEW JERSEY
West Coast Distributors: GALEN COMPANY, Richmond, Calif.

122J

FROM THE PAINTING BY HENRY INMAN

COURTESY NEW YORK HOSPITAL

Valentine Mott

1785 1865

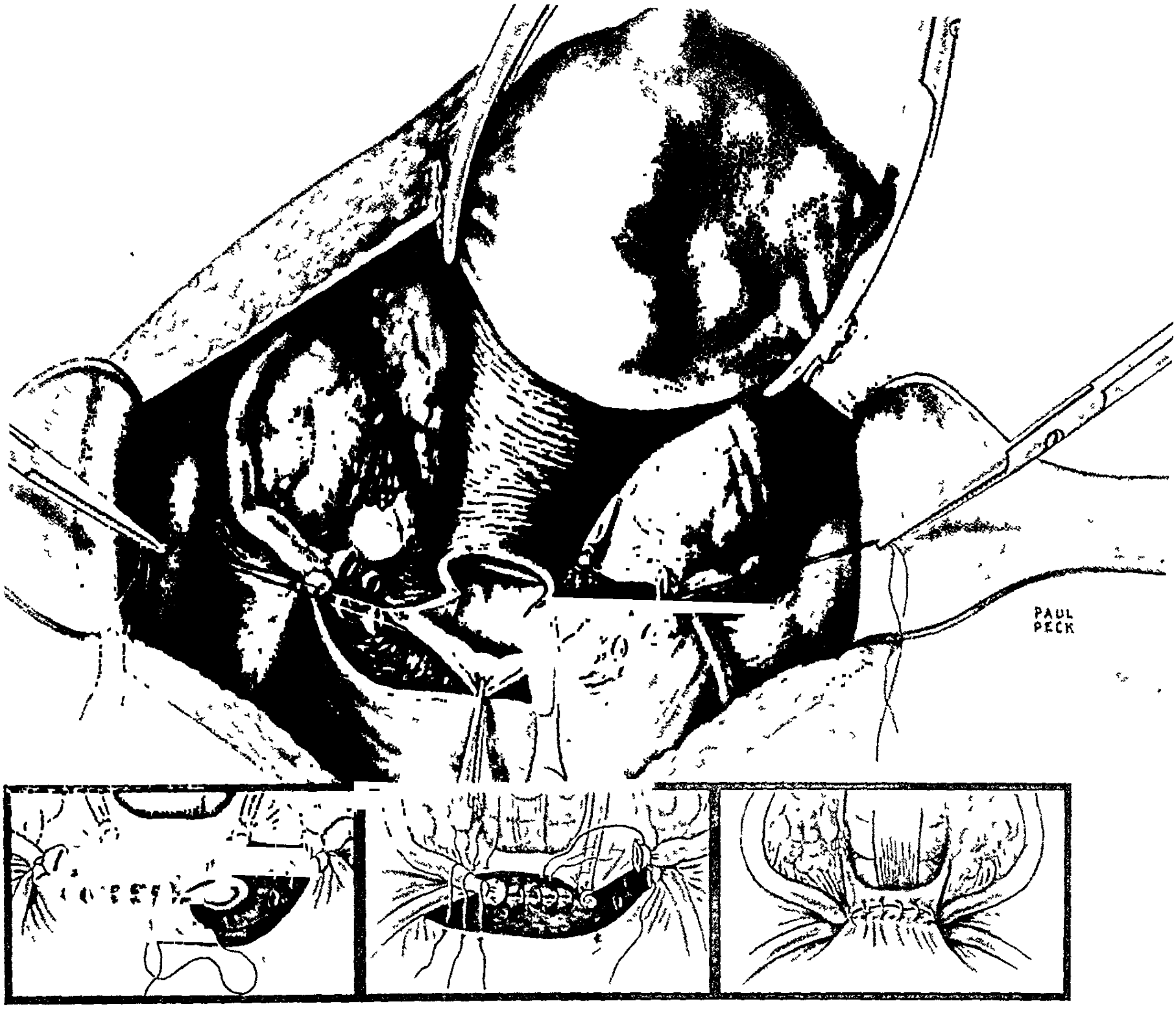
Celebrated surgeon of the 19th Century active for long periods in the College of Physicians and Surgeons and at New York Hospital

In 1810 at [illegible] Dr Mott became Professor of Surgery in Columbia College continuing through its merger with the College of Physicians and Surgeons He was intermittently Professor of Surgery until 18[illegible]2 between lengthy trips to Europe and the East

His association with New York Hospital began in 1817 as attending surgeon In 1837 he became consulting surgeon He was a president of New York Academy of Medicine and the New York Inebriate Asylum consulting surgeon at Bellevue and professor of surgery at University of New York

From the Series Great American Surgeons Published By

ETHICON SUTURE LABORATORIES, DIVISION OF JOHNSON & JOHNSON, NEW BRUNSWICK N J



Advances in Ob. & Gyn. Suturing

NEW CLINICAL PROCEDURES FAVOR NEEDLE SUTURES

Sutures swaged to eyeless needles are being more widely adopted for use in delicate tissues by Gynecologists. Many Obstetricians have changed entirely to eyeless needles for episiotomy closure.

This trend has been revealed by Ethicon's recent six-month study in many prominent hospitals. As a result, a new group of 13 Ob. and Gyn. eyeless needle sutures has been developed. There are four new needles, swaged to chromic gut, sizes 3-0 to 2.

The clumsy bulk of the eyed needle, combined with the doubled strand, with its attendant tearing or ripping of tissue, has influenced the more meticulous technicians to take advantage of the refinements derived from the eyeless needle.

Many surgeons have objected to eyed needles, used out of necessity, which are often too large, bent, dull, or even rusted. The Atraloc eyeless needle eliminates these difficulties as well as the time wasted in rethreading needles at critical moments.

The Atraloc eyeless needle draws a single strand of suture through the tissues, eliminating confusion and minimizing trauma in the often difficult and potentially dangerous suturing encountered in Ob. and Gyn. work. It is carefully engineered and is made by highly skilled craftsmen.

All Ethicon Ob. and Gyn. eyeless needles are swaged to Ethicon's Tru-gauged, Tru-chromicized Surgical Gut, noted for its superior strength and flexibility.

Swaged Needles At No Extra Cost

These new Ethicon sutures with swaged needles are supplied to hospitals at no extra cost over the regular Standard Tubes of Surgical Gut. They are delivered in the new, unbreakable metal Sterile Pack canisters which guarantee sterility of tube exteriors.

Increasing Preference for Eyeless Needles

A trend toward eyeless needles is evident in Ob. & Gyn. suturing. Leading surgeons in this field prefer a non-traumatizing needle, they reported to the Ethicon Development and Survey Department.

The illustrations at the right show the contrast between the old style eyed needle and the new streamlined, eyeless Atraloc needle supplied by Ethicon.

The eyed needle does greater injury to tissue because it pulls a looped suture in its wake. The eyeless needle causes minimal trauma by pulling a single strand, slightly smaller than the needle.

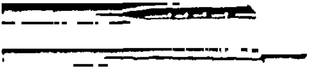
EYED NEEDLE

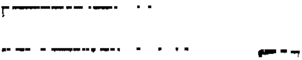
ATRALOC NEEDLE

Ethicon's New Seamless Swaged Needles

The newest improvement in swaging eyeless needles is the Ethicon seamless swage, shown contrasted with the conventional swage in the illustrations at the right.

As shown, the swage has no seam. The suture is inserted in a bored aperture in high-tempered steel, then locked by compression. No rough edges or gaps to scrape tissue. This new swage is only one-quarter as long as the conventional swage, yet tests show superior holding power.


CONVENTIONAL SWAGE

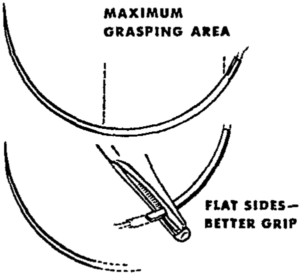

ETHICON SEAMLESS SWAGE

Better Needles for Today's Finer Suturing

In addition to the seamless swage, Ethicon's new Atraloc Needles offer the surgeon these additional advances and improvements.

Uniform high temper from end to end: Reduced bending: Rigidity without brittleness: greater strength throughout. The shorter swage means a maximum grasping area with parallel flattened sides for the needle holder. No turning of needle.

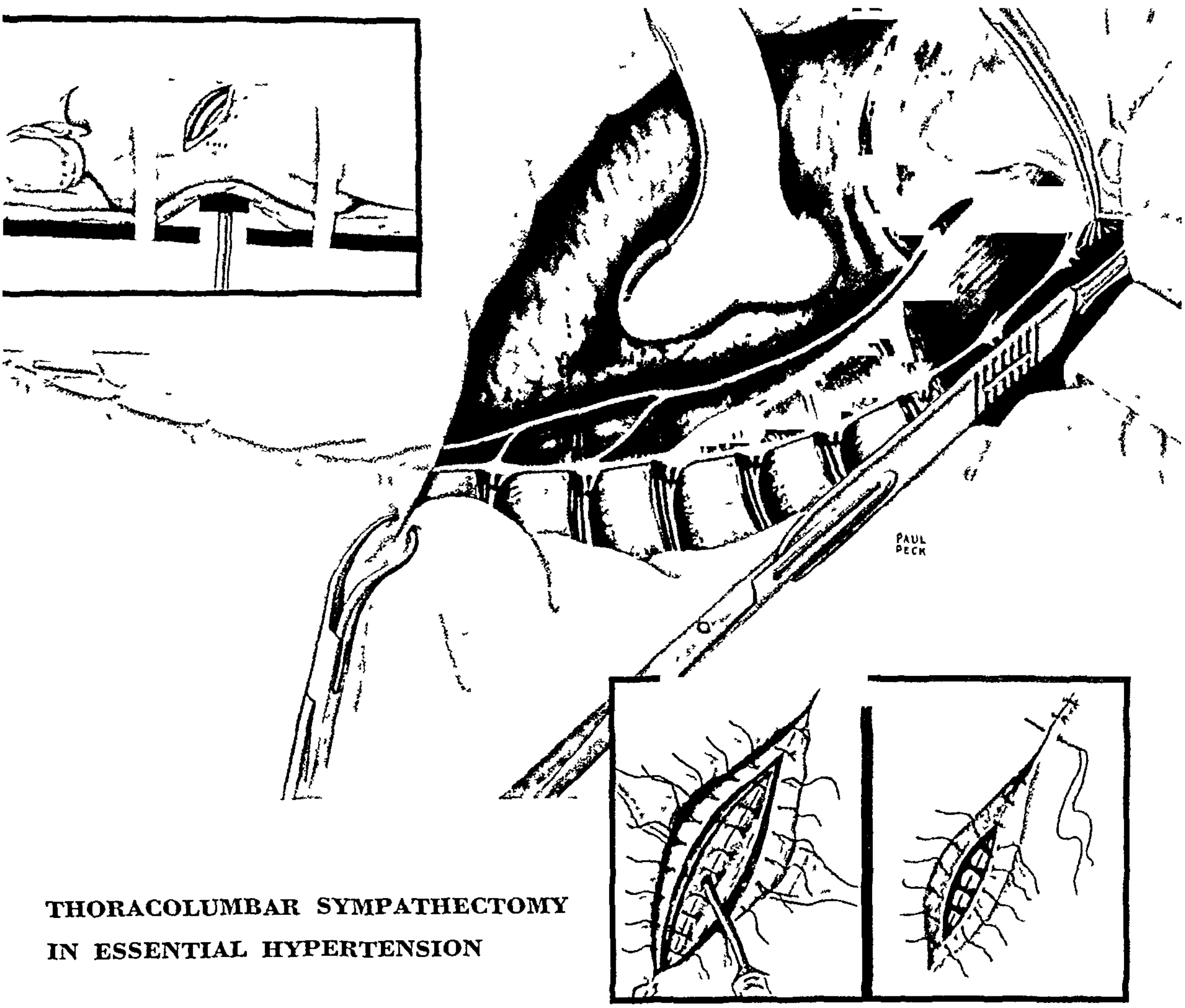
All points are hand honed, giving uniform sharpness and long taper.



POINTS HAND-HONED FOR SHARPNESS

COMPLETE LITERATURE SENT ON REQUEST

ETHICON



THORACOLUMBAR SYMPATHECTOMY IN ESSENTIAL HYPERTENSION

Silk and Cotton Sutures

SILK—Prepared especially for the meticulous demands of the silk technic. You get more intrinsic strength and minimal tissue reaction with Ethicon's Tru-Formed Black Braided Silk Sutures.

Ethicon Silk forms smooth, firm knots. It has minimal adherence to tissue.

Ethicon Silk is non-capillary, serum-proof, non-toxic, and strictly U.S.P. gauge.

Ask your O.R. Supervisor for Ethicon Silk.

COTTON—Ethicon Cotton, U.S.P., is the culmination of exhaustive laboratory and clinical study. It is specially prepared from imported 100% Egyptian long staple fiber. No talcum powder, harsh fillers, or harmful dyes are used. It is free from lint and irregularities.

Tensile strength is 10% to 30% greater than ordinary cotton. Sizes are U.S.P.: 5-0, 4-0, 3-0, 2-0, 0, 1 and 2. If you are a cotton man, try Ethicon Twisted Cotton.

ETHICON
Sutures

ETHICON SUTURE DIVISION

Division of Johnson & Johnson New Brunswick, N. J. World's Largest Manufacturer of Surgical Gut
Suture Laboratories at New Brunswick, N. J.; Chicago, Ill.; Brazil; Argentina; England, Australia
COPYRIGHT 1948, JOHNSON & JOHNSON • PRINTED IN U S A

The most potent androgen...

PERANDREN

(testosterone propionate U.S.P. XIII)

IN THE MALE 'The principal usefulness has been as a replacement therapy ."[1] when functional or organic testicular deficiency exists

The chief indications are the male climacteric, hypogonadism, and impotence due to glandular causes

Dosage is from 10 to 25 mg one to three times a week Perandren should be discontinued or the dose decreased if priapism supervenes or if mental excitement occurs The amount administered to prepuberal boys should be insufficient to precipitate puberty

IN THE FEMALE " the use of androgens in women has resulted in more effective management of a variety of clinical disorders '[2]

These include the menopausal syndrome, functional uterine bleeding and dysmenorrhea

Dosage should not exceed 300 mg per month Perandren should be discontinued or the dose decreased if signs of masculinization appear

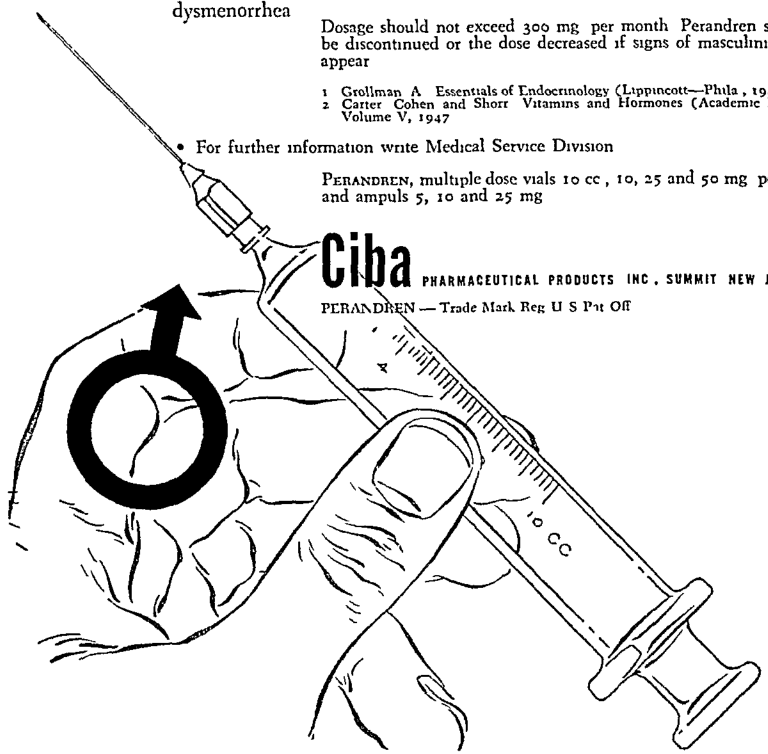
1 Grollman A Essentials of Endocrinology (Lippincott—Phila , 1944)
2 Carter Cohen and Shorr Vitamins and Hormones (Academic Press), Volume V, 1947

- For further information write Medical Service Division

PERANDREN, multiple dose vials 10 cc , 10, 25 and 50 mg per cc , and ampuls 5, 10 and 25 mg

Ciba PHARMACEUTICAL PRODUCTS INC . SUMMIT NEW JERSEY

PERANDREN — Trade Mark Reg U S Pat Off



MANDELAMINE

REG U S PAT OFF

Urinary Antiseptic of Choice—

in prolonged therapy or acute cases

MANDELAMINE* continues to be acknowledged [1,2,3] as a urinary antiseptic of choice not only in typical uncomplicated cases, but also more resistant conditions requiring treatment over long periods.

in prolonged therapy—

Sustained Effectiveness and Safety When Therapy Must Be Prolonged. MANDELAMINE, because of its undiminished antibacterial effectiveness, patient-acceptance, and virtual freedom from untoward reactions, is a logical choice when chemotherapy must be prolonged,[1,4] or when the infection becomes resistant to other medication.

in acute cases—

Rapid Results in Common Urinary Infections. Carroll and Allen[3] obtained successful results in approximately 74 per cent of 200 cases of common urinary-tract infections—often in as few as three days.

SUPPLIED: Enteric-coated tablets of 0.25 Gm. (3¾ grains), bottles of 120, 500, and 1,000.

6 OUTSTANDING FEATURES

1. No gastric upset
2. No dietary or fluid regulation
3. No supplementary acidification (except when urea-splitting organisms occur)
4. Wide antibacterial range
5. No danger of drug-fastness
6. Simplicity of regimen—3 or 4 tablets, t.i.d.

1. Butt, A. J.: J. Florida M. A. 35: 430 (Jan.) 1949.
2. Merricks, J. W.: West Virginia M. J. 44: 157 (June) 1948.
3. Carroll, G., and Allen, H. N.: J. Urol. 55: 674 (June) 1946.
4. Scudi, J. V., and Duca, C. J.: J. Urol. (Feb.) 1949.

*MANDELAMINE is the registered trademark of Nepera Chemical Co., Inc. for its brand of Hexydaline (methenamine mandelate)

NEPERA CHEMICAL CO., INC.

Manufacturing Chemists

NEPERA PARK • YONKERS 2, N. Y.

a new and outstanding development in penicillin therapy

PENICILLIN S-R*

Parke-Davis

COMBINED SOLUBLE AND REPOSITORY PENICILLIN

higher INITIAL LEVELS

prolonged MAINTENANCE LEVELS

extra MARGIN OF EFFECTIVENESS

ease of flow
use any syringe without clogging

higher initial levels

A 1-cc intramuscular injection produces serum levels of 4 0 units per cc—a value 133 times higher than the commonly accepted therapeutic level, 0 03 units per cc

quicker maximal therapeutic levels

Within a half hour or less after the injection, a high concentration of penicillin is found in the tissues

prolonged high maintenance levels

For twenty four hours or longer, a single injection continues to provide effective therapeutic levels

better control of infection

Rapid onset and prolonged maintenance of higher levels means more effective antibacterial action than possible with penicillin in retardant vehicles

extra margin of effectiveness

Higher levels quickly obtained permit early dominance over infecting organisms and diminish likelihood of penicillin fastness

ease of flow

Penicillin S R contains no oil, no wax, no added suspending or dispersing agents to impede injection or clog needle and syringe

additional advantages of PENICILLIN S-R

PREPARATION:
Easily and quickly prepared
Aqueous diluent
No vigorous shaking

ADMINISTRATION:
Free flowing
Quickly injected
No special type syringe

CONVENIENCE:
Syringe and needle need not be dry
No plugging of needles (20 or 21 gage)
Syringe and needles easily cleaned

TOLERANCE:
No sensitizing diluents
No added suspending agents
Completely absorbed
Minimal pain

PENICILLIN S-R is supplied in both one dose (400 000 units) and five-dose rubber-diaphragm-capped vials When diluted according to directions (with Water for Injection U S P Normal Saline Solution U S P or 5 per cent Dextrose Injection U S P), each cc contains 300 000 units of crystalline procaine penicillin-G and 100 000 units of buffered crystalline sodium penicillin-G The one dose vial is also available with an accompanying ampoule of Water for Injection U S P if desired Potency of the suspension is maintained for seven days at refrigerator temperatures

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN

MEDICAMENTA VERA

*Trademark

PROMPT REPAIR SERVICE

Cutting Loops Expertly Rebuilt. Reasonable. Send us your burned Loops.

BAKELITE SHEATHS REPLACED

We manufacture and Repair all types of Electro-Surgical Electrodes & Accessories. Prices upon request.

GREENWALD CO., INC.
DEPT. E GARY, INDIANA

Sixteenth Edition—
Stedman's
Practical
Medical
Dictionary

SANS TACHE

Edited by NORMAN B. TAYLOR, M.D.
University of Toronto

- ▶ Hundreds of new titles and subtitles added, hundreds rewritten, obsolete terms omitted.
- ▶ Continues to be the "last word" in the pronounciation, spelling, and meaning of medical terms.

1292 pages *23 plates* *$7.50*

THE WILLIAMS & WILKINS CO.
Mt. Royal and Guilford Aves. • Baltimore 2, Md.

RADON

When interstitial radiation is indicated, the ALL GOLD radon implant is recommended.

Our Radon Implants are ALL GOLD—24 Karat—and excellent for intratumoral implantation.

High temperature sterilization is possible with utmost safety.

Accurate dosage is assured because the ALL GOLD radon implant is sold with a guarantee as to radon content at hour of use.

•

Prices and Literature on Request.

RADIUM CHEMICAL COMPANY • Inc.

570 Lexington Ave., New York, 22, N. Y.

Chicago: Marshall Field Annex Building
Los Angeles: 3723 Wilshire Boulevard

A Significant Advance in ANTIBIOTIC THERAPY

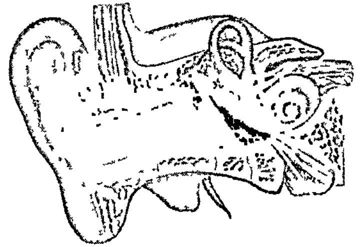
Note these five favorable attributes of Dihydrostreptomycin Merck

(1) Low incidence of vestibular disturbances
(2) Significantly less toxic
(3) Less frequent allergic manifestations
(4) Highly purified
(5) Undiminished antibacterial activity against *Mycobacterium tuberculosis*

A NEW, highly purified antibiotic, chemically distinct from streptomycin, with greatly reduced neurotoxicity, Dihydrostreptomycin Merck is especially useful in cases requiring relatively high dosage, such as miliary tuberculosis and tuberculous meningitis.

It can be used interchangeably for intramuscular therapy with Streptomycin Calcium Chloride Complex Merck or other forms of streptomycin.

Descriptive literature is yours for the asking



LOW INCIDENCE OF EIGHTH CRANIAL NERVE DAMAGE

DIHYDROSTREPTOMYCIN MERCK

(supplied as the sulfate)

MERCK

MERCK & CO., Inc. *Manufacturing Chemists* RAHWAY, N. J.

RETROPUBIC URINARY SURGERY

by Terence Millin, F.R.C.S.

Genito-Urinary Surgeon, London

Gives in detail the methods employed in the retropubic approach to a number of surgical problems

Prostatectomy
Stress Incontinence in Women
Prostatic Obstruction
Fibrous and Calculous Prostate
Carcinoma of the Prostate and Bladder
Pre- and Post-operative Care
Anesthesia

215 pp., 163 figs. $7.00

The Williams & Wilkins Co.

Mt. Royal & Guilford Aves., Baltimore 2, Md.

FEVER–

WHAT TO DO FOR IT

There is no better way of meeting the febrile state than by the administration of

Kalak®

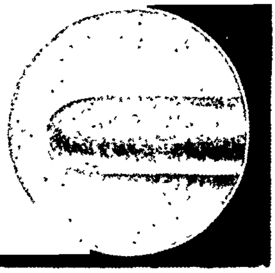
It is an invitingly pleasant alkaline drink mildly hypertonic and supplying the principal basic salts of which the animal body's alkali reserve is composed.

Kalak stands in good stead as an aid in neutralizing the acidosis of disease and that incident to various drug therapies.

Available at all pharmacies.

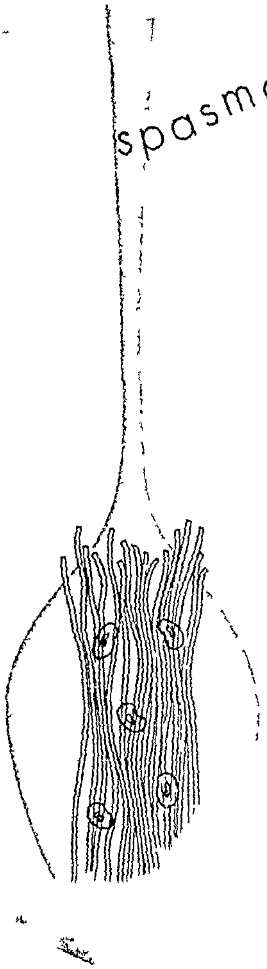
Kalak Water Co. of New York, Inc.
30 Rockefeller Plaza
New York 20, New York

RADON SEEDS



FOR safety and reliability use composite Radon seeds in your cases requiring interstitial radiation. The Composite Radon Seed is the only type of metal Radon Seed having smooth, round, non-cutting ends. In this type of seed, illustrated here highly magnified, Radon is under gas-tight, leak-proof seal. Composite Platinum (or Gold) Radon Seeds and loading-slot instruments for their implantation are available to you exclusively through us. Inquire and order by mail, or preferably by telegraph, reversing charges.

THE RADIUM EMANATION CORPORATION
GRAYBAR BLDG. Telephone MU 3-8636 NEW YORK, N. Y.



spasmolysis

spoonfed

For your discriminating choice of a spasmolytic agent, these striking characteristics of Robins' Donnatal Elixir are particularly noteworthy·

- It's a *superior* spasmolytic in the most varied manifestations of visceral vagotonia—*it suits* the youngest, oldest, or the most finicky "taste."
- It provides the principal *natural* belladonna alkaloids in *unvarying optimal* ratios—is compatible with many adjuvant medications.
- *It comprehensively combines* peripheral and central sedation—for cases of either somatogenic or psychogenic etiology.
- It's potent spasmolysis . . . **spoonfed!**

Each 5cc of Donnatal Elixir contains

Hyoscyamine Sulfate	0.1037 mg
Atropine Sulfate	0.0194 mg
Hyoscine Hydrobromide	0.0065 mg
Phenobarbital (¼ gr)	16.2 mg

• • • • elixir

Also available as Donnatal Tablets and Donnatal Capsules

A-H-Robins

A. H. Robins Co., Inc.

Ethical Pharmaceuticals of Merit since 1878

Richmond 20, Va.

FOR WIDELY APPLICABLE READILY ACCEPTED SPASMOLYTIC THERAPY

in

water-soluble

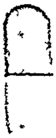
vitamin

therapy

n above the mark to hit th ma

(ers

"Err on the side of giving an excess rather than giving too little,"[1] urges Jolliffe on vitamin supplementation. Says Spies: "[Prescribe it] too soon rather than too late."[2] • In one small capsule,



'Robins' Allbee with C delivers the B-factors in two to fifteen times the minimum daily requirement* plus vitamin C in eight times the minimum daily requirement • Unmistakably, Allbee with C provides a ready means for water-soluble vitamin "saturation" therapy.

*or other official recommendations.

each capsule contains

Thiamine Hydrochloride (B_1)	**15 mg.**
Riboflavin (B_2)	**10 mg.**
Calcium Pantothenate	**10 mg.**
Nicotinamide	**50 mg.**
Ascorbic Acid (C)	**250 mg.**

1. Jolliffe, N
New York State J Med
41 1363 1941

2. Spies T D:
J A M A
122 299, 1943

A.H Robins Co., inc. Richmond 20, Va.
ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878

allbee WITH C Robins

During Pregnancy

TO BUILD BLOOD AND IMPROVE NUTRITION

HYPOCHROMIC ANEMIA is so common during pregnancy that some authorities advocate routine administration of medicinal iron to all pregnant women. Cytora, in the recommended dosage, supplies an adequate amount of iron for the increased requirements of pregnancy *plus* folic acid for its recently reported property of aiding gastro-intestinal function *and* vitamin C and B-complex factors—vitamins which are said to be probably of greater importance to the health of the pregnant woman than any of the others. Moreover, the pharmaceutical skill exercised in compounding Cytora tablets assures optimal absorption and minimizes gastric disturbances. Cytora is available in bottles of 100, 250, and 1000 tablets.

ORGANON INC. (*formerly known as* ROCHE-ORGANON INC.) ORANGE, N. J.

CYTORA

'Organon'

DAILY DOSE (6 TABLETS) PROVIDES:

Ferrous Sulfate	600.0 mg
Folic Acid	4.5 mg
Liver Concentrate	900.0 mg
Vitamin C	150.0 mg
Vitamin B_1	6.0 mg
Vitamin B_2	6.0 mg
Vitamin B_6	3.0 mg
Niacinamide	30.0 mg
Calcium Pantothenate	6.0 mg

plus other factors naturally present in liver concentrate

M.—Cytora — Reg U S Pat Off

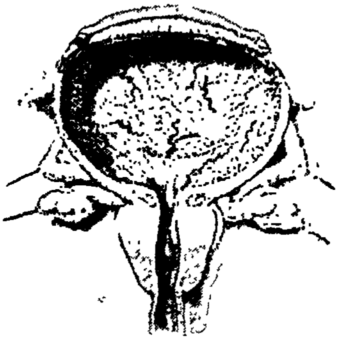
PATIENT under TREATMENT

ENJOYS

Gratifying Relief

from distressing

URINARY SYMPTOMS



Distressing symptoms of urinary tract infection such as urinary frequency, pain and burning on urination can be relieved promptly in a high percentage of patients through the simple procedure of administering Pyridium orally.

With this easy-to-administer and *safe* urinary analgesic, physicians can often provide their patients with almost immediate relief from distressing urinary symptoms during the time that other therapeutic measures are directed toward alleviating the underlying condition.

Pyridium is virtually nontoxic in therapeutic dosage and can be administered concomitantly with streptomycin, penicillin, sulfonamides, or other specific therapy.

The complete story of Pyridium and its clinical use is available on request.

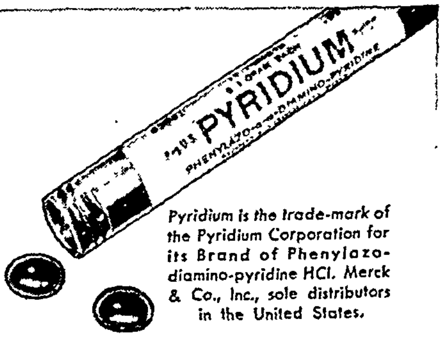
PYRIDIUM®

(Brand of Phenylazo-diamino-pyridine HCl)

MERCK & CO., Inc. RAHWAY, N. J.

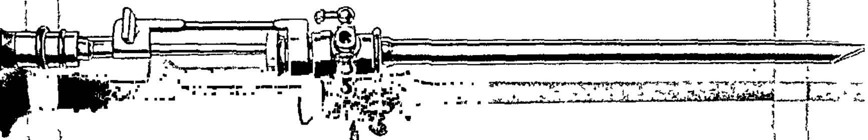
Manufacturing Chemists

In Canada: MERCK & CO., Ltd. Montreal, Que.



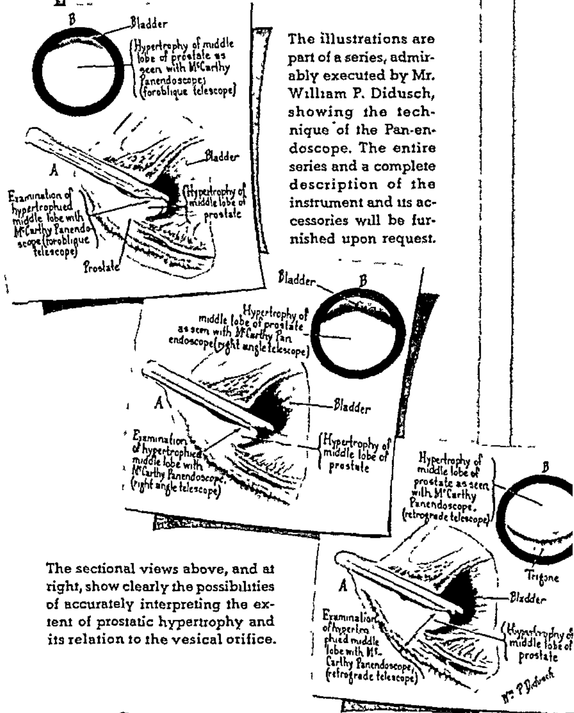
Pyridium is the trade-mark of the Pyridium Corporation for its Brand of Phenylazo-diamino-pyridine HCl. Merck & Co., Inc., sole distributors in the United States.

McCARTHY FOROBLIQUE PAN-ENDOSCOPE



This appropriately named cystoscope possesses such broad utility that it has become one of the most widely used instruments in urology.

Essentially the armamentarium consists of straight sheaths, a foroblique telescope and a bridge assembly for relating these elements. Sheaths are available in sizes 16 to 30 Fr. The telescope is the well-known McCarthy Foroblique* System noted for its natural, "amphitheatre", visual characteristics. Supplementary retrograde and right angle examining telescopes are also available for detailed inspection of all parts of the bladder and prostatic orifice.


B
Bladder
Hypertrophy of middle lobe of prostate as seen with McCarthy Panendoscope (foroblique telescope)
A
Bladder
Examination of hypertrophied middle lobe with McCarthy Panendoscope (foroblique telescope)
Hypertrophy of middle lobe of prostate
Prostate
Bladder
B
Hypertrophy of middle lobe of prostate as seen with McCarthy Panendoscope (right angle telescope)
A
Bladder
Examination of hypertrophied middle lobe with McCarthy Panendoscope (right angle telescope)
Hypertrophy of middle lobe of prostate
Hypertrophy of middle lobe of prostate as seen with McCarthy Panendoscope. (retrograde telescope)
B
Trigone
A
Bladder
Examination of hypertrophied middle lobe with McCarthy Panendoscope (retrograde telescope)
Hypertrophy of middle lobe of prostate
Wm P Didusch

The illustrations are part of a series, admirably executed by Mr. William P. Didusch, showing the technique of the Pan-endoscope. The entire series and a complete description of the instrument and its accessories will be furnished upon request.

The sectional views above, and at right, show clearly the possibilities of accurately interpreting the extent of prostatic hypertrophy and its relation to the vesical orifice.

*"Foroblique" is our registered trade mark to designate our obliquely forward visual telescopic system.

ESTABLISHED IN 1900 BY REINHOLD H. WAPPLER

FREDERICK J. WALLACE
PRESIDENT

AMERICAN CYSTOSCOPE MAKERS, INC.
1241 LAFAYETTE AVE. NEW YORK 59, N. Y.

the 16 Fr.

McCarthy Electrotome

This newly developed modification of the McCarthy Electrotome was designed for use on infants or adolescents or in cases involving very small urethras.

It employs a working element with standard McCarthy rack and pinion motion, reduced in size to fit the 16 Fr. Berry sheath, and a miniature McCarthy Foroblique telescope. A specially designed obturator accommodates the sheath, which contains a rotating water inlet. The cutting element is a loop of fine tungsten wire .010" in diameter, shaped to fit the small sheath. Since it carries a high current density per unit of area, it cuts and coagulates at very low settings (25 for cutting and 35 for coagulating, with the C-263 Wappler Surgical Unit). Two sheaths and extra loops are supplied with the instrument.

Full information sent on request

American Cystoscope Makers, Inc.

1241 LAFAYETTE AVE. • FREDERICK J WALLACE, President • NEW YORK 59, N.Y.

AMERICAN UROLOGICAL ASSOCIATION

OFFICERS 1948–1949

President—Dr. Charles C. Higgins, Cleveland Clinic, Cleveland, Ohio
President-Elect—Dr. Carl F. Rusche, 906 Taft Building, Hollywood, California
Past-President—Dr. Herbert H. Howard, 270 Commonwealth Avenue, Boston, Mass.
Secretary—Dr. Thomas D. Moore, 899 Madison Ave., Memphis, Tenn.
Treasurer—Dr. George C. Prather, 1180 Beacon Street, Brookline, Mass.
Historian—Dr. Wirt B. Dakin, 523 W. Sixth St., Los Angeles, California

EXECUTIVE COMMITTEE

New England Section—Dr. Roger C. Graves, 12 Bay State Rd., Boston, Mass.
Alternate—Dr. Fletcher H. Colby, 262 Beacon St., Boston, Mass.
New York Section—Dr. George W. Fish, 755 Park Avenue, New York, New York
Alternate—Dr. Augustus Harris, 306 Park Place, Brooklyn, New York
Mid-Atlantic Section—Dr. Charles H. deT. Shivers, 121 S. Illinois Ave., Atlantic City, N. J.
Alternate—Dr. Ralph M. LeComte, 1801 Eye St., N.W., Washington, D. C.
Southeastern Section—Dr. Hamilton W. McKay, 121 W. Seventh St., Charlotte, N. C.
Alternate—Dr. J. Ullman Reaves, 303 Van Antwerp Bldg., Mobile, Ala.
North Central Section—Dr. William J. Baker, 7 West Madison Street, Chicago, Illinois
Alternate—Dr. Carroll C. Hyde, 122 N. Lafayette Blvd., South Bend, Ind.
South Central Section—Dr. R. Lee Hoffmann, 1019 Professional Bldg., Kansas City, Mo.
Alternate—Dr. H. Fay H. Jones, 808 Donaghey Bldg., Little Rock, Ark.
Western Section—Dr. Dudley P. Fagerstrom, 710 Medico-Dental Bldg., San Jose, Calif.
Alternate—Dr. A. J. Scholl, 1930 Wilshire Blvd., Los Angeles, Calif.

Sections of the American Urological Association

NEW ENGLAND SECTION

President—Dr. Edward L. Peirson, 374 Essex Street, Salem, Mass.
Secretary-Treasurer—Dr. Richard Chute, 330 Dartmouth Street, Boston 16, Mass.
Executive Committee—Chairman, Dr. George C. Prather, 1180 Beacon Street, Brookline 46, Mass.; Dr. John P. Bowler, Hitchcock Clinic, Hanover, N. H.; Dr. Winthrop M. Flagg, 49 South Winooski Ave., Burlington, Vt.; Dr. Ernest K. Landsteiner, 4 George St., Providence, R. I.; Dr. Samuel A. MacDonald, 1414 Drummond St., Montreal, P. Q., Canada; Dr. Donald F. Marshall, 142 High St., Portland, Maine; Dr. C. H. Neuswanger, 89 N. Main St., Waterbury, Conn.; Dr. Bancroft C. Wheeler, 27 Elm St., Worcester, Mass.

NEW YORK SECTION

President—Dr. Francis P. Twinem, 901 Lexington Ave., New York, N. Y.
Vice-President—Dr. Herbert M. Ill, 42 Woodland Ave., Glen Ridge, N. J.
Secretary—Dr. John N. Robinson, 755 Park Ave., New York, N. Y.
Treasurer—Dr. Oscar P. Schoenemann, 848 Carroll St., Brooklyn, N. Y.
Executive Committee—Dr. John K. de Vries, 144 S. Harrison St., East Orange, N. J.; Dr. George W. Fish, 755 Park Ave., New York, N. Y.; Dr. Augustus L. Harris, 306 Park Place, Brooklyn, N. Y.; Dr. Robert S. Hotchkiss, 65 E. 66th St., New York, N. Y.

NORTHEASTERN SECTION

President—Dr. James C. McClelland, 170 St. George St., Toronto, Ontario
President-Elect—Dr. A. L. Parlow, Medical Arts Bldg., Rochester, New York
Past President—Dr. George E. Slotkin, 333 Linwood Ave., Buffalo, New York
Secretary-Treasurer—Dr. Albert M. Crance, 525 S. Main St., Geneva, N. Y.
Executive Committee—Dr. William A. Barrett, 506 Med. Arts Bldg., Pittsburgh, Pa.; Dr. J. Victor Berry, 180 Metcalfe St., Ottawa, Ont.; Dr. John L. Hamilton, 7086 Jenkins Arcade, Pittsburgh, Pa.; Dr. William J. Kennedy, 86 N. Main St., Gloversville, N. Y.; Dr. S. A. MacDonald, 1414 Drummond St., Montreal, Que.

NEW YORK

Archie L. Dean, 30 E. 40 St., New York City 16
John Newbold Robinson, 180 Fort Washington Ave., New York City 32
E. King Morgan, 52 Remsen St., Brooklyn 2
William A. Milner, 75 Willett St., Albany
Hans R. Sauer, Roswell Park Memorial Institute, 663 N. Oak St., Buffalo 3
W. W. Scott, Medical Arts Bldg., Rochester
Judson B. Gilbert, 1414 Union St., Schenectady 8

NORTH CAROLINA

John E. Dees, Duke University, Durham

OHIO

C. C. Higgins, Cleveland Clinic, Euclid Ave. at 93 St., Cleveland 6

OKLAHOMA

Anson L. Clark, 514 Medical Arts Bldg., Oklahoma City

PENNSYLVANIA

Edward W. Campbell, 1318 Medical Arts Bldg., 16th and Walnut Sts., Philadelphia

TENNESSEE

Samuel L. Raines, 188 S. Bellevue, Memphis 4

TEXAS

R. E. Van Duzen, 721 Medical Arts Bldg., Dallas 1

VIRGINIA

Samuel A. Vest, University of Virginia Hospital, University Station, Charlottesville

WASHINGTON

Alexander B. Hepler, 752 Stimson Bldg., Seattle 1

WISCONSIN

Walter M. Kearns, 238 W. Wisconsin Ave., Milwaukee

CANADA

ONTARIO

Carl Aberhart, 1012 Medical Arts Bldg., Toronto 5

QUEBEC

Magnus I. Seng, Suite 615, 1538 Sherbrooke St., West, Montreal

INSTRUMENT COLLECTION COMMITTEE

The Instrument Collection is made up of urologic instruments and devices given or lent to the American Urological Association. The Collection is to be kept permanently in the Army Medical Museum.

All gifts or loans to the Collection may be sent C.O.D. to Dr. William P. Herbst, 1801 Eye St., N. W., Washington 6, D. C.

J. A. Campbell Colston
William P. Herbst
Thomas J. Kirwin
A. J. Scholl
Montague L. Boyd, Chairman

NOMENCLATURE COMMITTEE

The Nomenclature Committee requests suggestions concerning additions to the published Urological Nomenclature, and also suggestions concerning changes in the present list of accepted diagnoses.

Clyde L. Deming
William J. Engel
John R. Hand
Hugh J. Jewett
Montague L. Boyd, Chairman

The Journal of Urology
Vol 61 No 3 March 1949
Printed in U S A

PHEOCHROMOCYTOMA WITH PAROXYSMAL HYPERTENSION[1]

GEORGE F HOCH

The clinical picture of medullary tumors of the suprarenal gland with paroxysmal hypertension has been described by many authors but it seems advisable to refresh our minds to its importance and the cure by surgical removal of the tumor

The medullary cells are turned blue by ferric chloride, and with chromie acid or its salts, a dark brown, as a result of this staining reaction the cells are called chromaffin cells The medullary tissue and the sympathetic ganglion cells have a common origin These develop from cell masses which have separated from the neural crest These ectodermal cells undergo differentiation along two paths—to sympathetic ganglion cells and to chromaffin tissue The larger mass becomes enveloped in cortical tissue to make the adrenal medulla Other smaller masses of chromaffin tissue becomes associated with the ganglia and plexuses of the sympathetic system Therefore if a symptomatic or clinical cure is not attained it may be possible that these extra-adrenal chromaffin rests may be the seat of a pheochromocytoma

CASE REPORT

A 51 year old white woman, who looked aged beyond her years, was admitted to the hospital for the first time in 1935 Her chief complaint was knife like abdominal pain associated with sweating, nausea and vomiting, aggravated by food and usually relieved by induced vomiting The provisional diagnosis was partial intestinal obstruction At operation a chronically infected gallbladder containing numerous small stones was removed At this time it was reported on her history that she had bilateral papilledema of undetermined cause Seven years ago she was admitted to another hospital where a diagnosis of hypertension was made Four years ago she began to have precordial pain radiating to both shoulders, down both arms and in neck and jaws With these attacks her vision became blurred For the past 2 years she had led an arm chair existence as she developed exertional dyspnea and ankle edema, although her appetite had been normal and she had lost considerable weight Her pulse rate on admission was 96, the blood pressure 130/100 The sedimentation rate was 16 m m , urea nitrogen 15 7 and cholesterol 198 The urine concentration was normal as were the blood count, urea clearance and blood serology An x ray of the heart showed slight left ventricular hypertrophy Repeated attacks were from 1 to 4 each day and the blood pressure varied between 130/80 to 240/150 Rice diet and nitrites did not relieve these paroxysms Intravenous pyelograms showed normal architecture of the renal pelves with a ptosis of the right kidney Perirenal insufflation was done, showing a tumor mass above the right kidney and a diagnosis of pheochromocytoma was made

---

[1] Read at annual meeting, American Association of Genito Urinary Surgeons, Skytop, Pa , May 12, 1948

During the course of the examination .05 mg. histamine phosphate was given subcutaneously with the following result.

HISTAMINE PHOSPHATE	B.P.	PULSE	
10.14			
10.15	70/50		Beginning headache, choking feeling, excruciating headache, profuse sweating, extreme pallor
10.16	220/160		
10.17	300/184	140	Same as above
10.18	296/170		Same but less severe
10.20	230/110		Less marked
10.21	154/94	130	Headache and pains gone
10.24	94/60	120	Exhaustion
10.25	104/80	120	Exhaustion

Dibenamine hydrochloride (dibenzyl betachlorethylamine hydrochloride) which has an adrenergic action, was given intravenously using a Y set. Seven milligrams per kilogram diluted in 300 cc 5 per cent glucose in normal saline in one arm and 5 per cent glucose in saline in the other arm. Start saline and switch to the Dibenamine solution. The Dibenamine was administered over a period of 1 hour in order to lessen any toxic reactions. There was an immediate drop in blood pressure with relief of her symptoms, accompanied by a feeling of well being. Her appetite improved and she regained some weight and strength. Histamine injected at this time failed to cause return of symptoms.

The toxic reactions of Dibenamine experimentally were:

1) Local tissue damage, especially if given intraperitoneally. The lethal dose for mice is 75–100 mg. compared to 400–500 mg. when given subcutaneously.

2) When given rapidly intravenously may cause clonic convulsions with coma lasting a few minutes to an hour or more. Doses of 35 mg. per kilo in cats are lethal in less than an hour.

3) Dibenamine does not effect bone marrow while the nitrogen mustards exert a toxic action on lymphoid tissue and bone marrow.

4) Dibenamine exhibits only a slight cumulative toxicity.

On November 26, 1947 a tumor of the right adrenal gland was removed. Avertin, nitrous oxide, oxygen and pentothal were the anesthetics of choice. The operation was done retroperitoneally, using a lumbar incision that started about 2½ cm. from the midline commencing at the eleventh rib and extending to the crest of the ileum about 4½ cm. from the midline. The twelfth rib was removed. The kidney and the overlying tumor were readily visualized. By retracting the kidney further downward the tumor was easily exposed. When freeing, the tumor was accidentally broken in one spot and the character of the material resembled that extruded from a papillary tumor of the kidney. The vessels were readily clamped and tied except at the upper portion where it was adherent to the diaphragm. The bleeding was partially controlled but it seemed advisable to put in one layer of Oxycel gauze. A rubber tissue drain was inserted and the wound closed. Her postoperative course was uneventful. Prior to operation 5 mg. of desoxycorticosterone acetate was given and continued *for the first 2 postoperative days together with a saline infusion.* Her postoperative blood pressure was 175/120 and eventually stabilized at 120/80, which it is at present.

A glucose tolerance test was done prior to operation and again after removal of the tumor and showed the characteristic change with the liberation of adrenalin in the circulation.

	FASTING	½ HR.	1 HR.	2 HRS.	3 HRS.
Preoperative	119	144	203	161	61
Postoperative	76	133	92	103	67

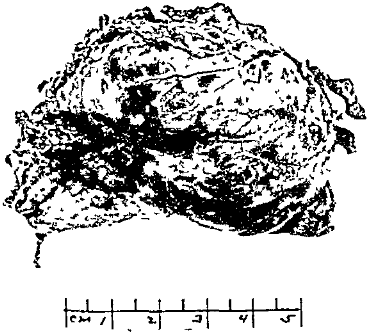


FIG 1

The postoperative histamine test was negative.

The pathological report was made by Dr. Leila Knox. The gross specimen consisted of a right adrenal tumor; the overall measurement was 9 by 7 by 25 cm. weighing 110 gm. The surface was smooth and the capsule thin. The color was pale yellow and the tumor was soft and very pliable, solid, without fibrous strands or stroma. A few minutes after exposure to 2 per cent potassium bichromate the color changed to dark brown.

Microscopic examination: Sections from the various portions of the growth showed almost exactly the same pathological picture. Nearly the whole growth was composed of very small cells with small nuclei a little larger than lymphocytes. These cells were closely packed together and frequently seemed to be surrounded by the connective tissue which carried the blood vessels so that there was a slight suggestion of a tumor divided into alveolar masses surrounded by blood vessels. There was no necrosis. Between these cells, Bielschowsky stains showed no connective tissue between the individual cells. In the chromate fixed tissue the cytoplasm may occasionally be seen to possess very finely granular brownish cytoplasm. This, combined with the fact that in the unfixed tissue a deep blackish brown color developed when potassium chromate solution was applied indicated that the tissue is of a chromaffin type.

This is not the usual morphology for a pheochromocytoma as the cells are much larger and the cytoplasm much more extensive in proportion to the nucleus but the staining reactions are probably of greater significance than the morphology in this case.

CONCLUSIONS

A case is reported of pheochromocytoma with removal of the adrenal tumor and cure.

The pathological picture is not that of the classical picture of a pheochromocytoma.

The use of Dibenamine for its adrenergic action is reported. Its possible use to prevent the sometimes fatal result at operation is suggested. The chemical formula of Dibenamine is N,N-dibenzyl-beta-chlorethylamine.

The Dibenamine was supplied by Dr. W. Gump of Givaudan-Delawanna Inc., New York.

N,N-dibenzyl-beta-chloroethylamine is being distributed for investigational use by the Smith, Kline and French Laboratories, Philadelphia, Pa. under the trademark 'Dibenamine.'

115 E. 61st St., New York, N. Y.

REFERENCES

Bauer, J. and Belt, E.: J. Clin. Endcrin., **7**: 30, 1947.
Beer, E., King, F. H. and Prinzmetal, M.: Ann. Surg., **106**: 85, 1937.
Brunschwig, A. and Humphreys, E.: J. A. M. A., **115**: 355, 1940.
Burrage, W. C. and Halstead, J. A.: Ann. Int. Med., **28**: 838, 1948.
Heath, F. K., Cahill, G. F. and Atchley, D. W.: J. A. M. A., **117**: 1258, 1941.
Hyman, A. and Mencher, W. H.,; J. Urol., **49**: 755, 1943.
Kvale, W. F., Roth, G. M., Clagett, O. T. and Dockerty, M. B.: Surg. Clin. No. Am., **24**: 922, 1944.
McCullagh, E. P. and Engel, W. J.: Ann. Surg, **116**: 61, 1942.
Nickerson, M., Goodman, L. S. and Nomaguchi, G. M.: J. Pharm. and Exp. Therap., **89**: 180, 1947.
Simeone, F. A. and Sarnoff, S. J.: J. Surg., **22**: 391, 1947.
Thorn, G. W., Hindle, J. A. and Sandmeyer, J. A.: Ann. Int. Med., **21**: 122, 1944.
Weiss, S., Robb, G. P. and Ellis, L. B.: Arch. Int. Med., **49**: 360, 1932.
Wells, A. H. and Boman, P. G.: J. A. M. A., **109**: 1176, 1937.

THE JOURNAL OF UROLOGY
Vol 61 No 3 March 1949
Printed in U S A

THE IMPORTANCE OF ACCURATE PATHOLOGICAL CLASSIFICATION IN THE PROGNOSIS OF RENAL TUMORS
SECOND REPORT[1]

N CHANDLER FOOT, G A HUMPHREYS AND WILLET F WHITMORE, JR

From the Department of Surgery (Surgical Pathology and Urology) of the Cornell University Medical College and the New York Hospital, and the Department of Urology of Memorial Hospital, New York, N Y

The problem of renal tumors has been clouded by the lack of a simple pathologic classification, such a one as should permit standardization of terminology to meet the needs both of the clinician and the pathologist In a paper published earlier this year the cases of renal tumors observed at the New York Hospital from 1932–1946 were collected and evaluated A pathologic classification of renal tumors based upon histogenetic and histologic criteria was therein proposed and was found to permit of a reasonable correlation between the pathologic type of tumor and the prognosis following nephrectomy To supplement the previous paper, we have reviewed all the cases of renal tumors seen at the Memorial Hospital during the years 1926 through 1947 inclusive and at the New York Hospital, during the years 1932 through 1946 inclusive A total of 338 cases was thus reviewed, many of these revealed advanced metastasis and were treated palliatively In 115 the diagnosis was accurately confirmed by operation or postmortem examination, as well as by clinical study and, in most, a complete follow-up record was available We have confined our survey to this small but well documented series of cases

PATHOLOGIC CRITERIA

The pathologic classification is that proposed in the previous paper The older terminology was found to be merely descriptive and frequently conflicting and confusing, since one might encounter two or more of its distinct and presumably different categories in selected sections from the same tumor in a single kidney We have classified renal tumors into four main groups (table 1) The essential part of this classification is comprised of the main groups designated by Roman numerals, while the less essential subgroups are numbered by the conventional Arabic numerals Those marked by lower case letters are more in the nature of explanation and correlation and are unessential

The reason for adopting the term "renal celled carcinoma" has been fully explained in the previous paper, further indication that it is accurate is afforded by the histology of the two varieties of renal adenoma One of these is clear celled and tubular, while the other is granular celled and arranged in solid masses and cords Both types are occasionally observed to occur simultaneously in the same kidney Obviously, the sub-varieties of renal celled carcinoma might arise from one or the other of these adenomas, neither of which is derived from suprarenal tissue Naturally, they might also originate from renal cells which became malignantly neoplastic In order to illustrate this, the photomicrographs (figs. 1, 2, 3) have been prepared from sections taken from a single kidney removed by nephrectomy at the New York Hospital.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass , May 17, 1948

The tumors of the conductive apparatus (pelvis, minor infundibulia and the distal portion of the collecting tubules) usually retain the architecture of transitional epithelium, histologically identical with that of the urinary bladder. The only exception is the tubular tumor of the renal pyramids which, since it arises in collecting tubules, maintains its resemblance to the epithelium of these. The nonmalignant tumor of the conductive apparatus is the transitional papilloma. The malignant variety may become epidermoid or, on rare occasions, adenocarcinomatous. Under nonneoplastic conditions metaplasia of transitional epithelium may lead to the development of epidermoid or, less frequently, mucous glandular forms. The epidermoid variety of carcinoma may exhibit early keratinization alone, or it may progress to the formation of keratinized "pearls" and prickle cells. Poorly differentiated carcinomas of the conductive system are often diffuse and infiltrative. Their elements may be small and resemble those of an inflammatory exudate.

TABLE 1. *Pathologic classification of renal tumors*

Group I.	Derived from excretory epithelium of the parenchyma.
	1. Adenoma
	a. Clear celled, tubular.
	b. Granular celled, solid or cords.
	2. Renal celled carcinoma
	a. Clear celled, hypernephroid, with cells arranged in solid cords (formerly "hypernephroma")
	b. Clear celled with cells arranged in tubules or papillary cysts (formerly "clear celled carcinoma")
	c. Granular cells arranged in papillary cysts (formerly "granular celled papillary adenocarcinoma")
	d. Clear or granular cells arranged in tubules only, found in cortex (formerly "tubular carcinoma")
Group II.	Derived from transitional epithelium of the conductive apparatus.
	1. Well differentiated, nonmalignant transitional papilloma.
	2. Transitional celled carcinoma
	a. Poorly differentiated, infiltrating transitional celled carcinoma.
	b. Epidermoid carcinoma of calyces and pelvis.
	c. Tubular carcinoma of pyramids. Usually desmoplastic (formerly "scirrhous carcinoma of kidney")
Group III.	Derived from embryonal rests.
	1. Predominantly epithelial growths derived from embryonal rests (?). Embryonal carcinoma.
	2. Embryonal tumors of mixed histology, including muscle. Wilms' tumor.
Group IV.	Derived from external tissue.
	Extrinsic tumors situated in perirenal capsule or metastatic to kidney (may invade kidney through direct extension)

The embryonal group of tumors is poorly understood. Its origin probably lies in that embryologic playground in the vicinity of the mesonephros, where muscular cells may creep in from neighboring somites, mesonephric elements persist from that primitive organ, or other forms of histologic transmigrations take place. As a consequence, there is a great diversity of architecture and disparity of the elements concerned in the make-up of these embryonal growths. One questions the advisability of further subdivision of embryonal tumors. Wilms' tumor bears his name and many aliases besides; though sometimes very mixed in composition, it may be relatively simple. It is most typical when it contains muscular elements. We have separated the mixed from the more homogeneous embryonal carcinoma because it appears to behave somewhat differently and to be a trifle less malignant. Whether these two types are extremes in a scale of differentiation in one group of embryonal carcinoma, or whether they have totally different origins is a question that has not been authoritatively answered.

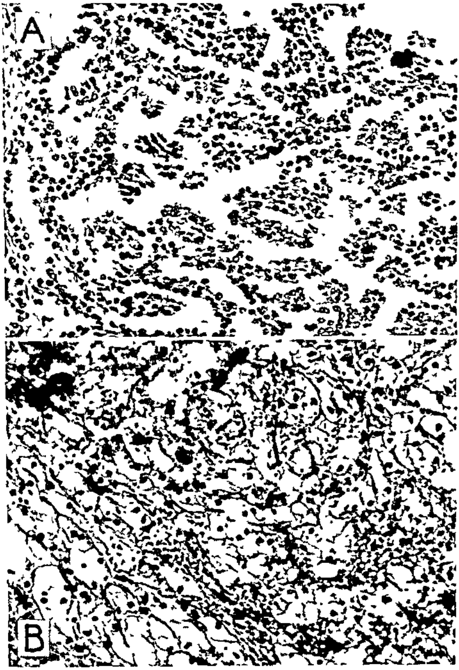


FIG. 1. *A*, papillary adenoma of kidney composed of small, comparatively clear cells arranged in tubules and papillae. *B*, solid clear celled area in renal celled carcinoma, cytoplasm vacuolar, nuclei small, isometric and pyknotic.

The extrinsic group of renal tumors includes growths originating in the muscular walls of the pelvis and ureters, in perirenal connective tissue and

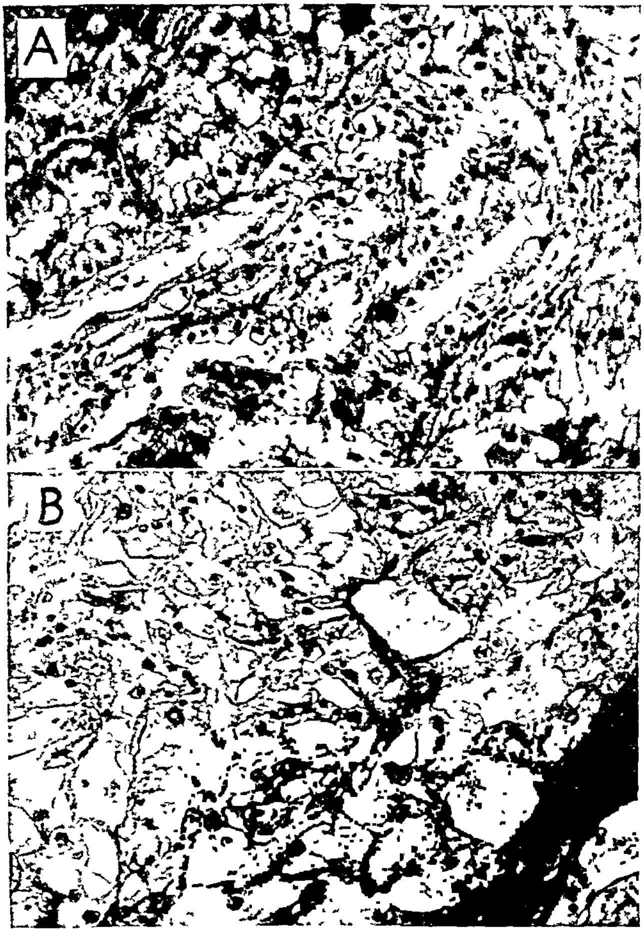


FIG. 2. *A*, more granular area in same tumor, cells larger, nuclei more vesicular and less isometric. *B*, tubular and papillary area in same tumor. Cells slightly granular, nuclei small, isometric and pyknotic.

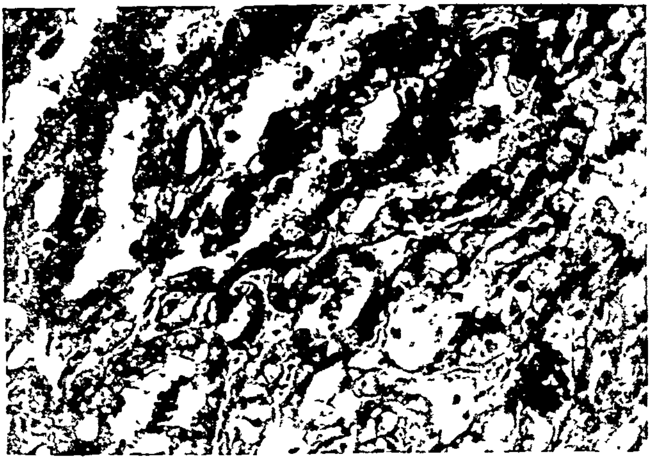


FIG. 3. Again from same tumor. Dark tubular area with dense granular cytoplasm contrasts with solid portion at lower right in which cells are almost clear and one of them shows a mitotic division.

fatty capsule, or in other organs from which they have invaded the kidney by metastasis or direct invasion. Although the term "extrinsic" is not entirely satisfactory, no better designation could be suggested. One of our collected examples of this group, for instance, proved to be a true cortical carcinoma of the suprarenal gland which directly invaded the upper pole of the kidney. It was valuable from the standpoint of comparison, for it differed histologically from clear celled carcinoma of renal origin and, furthermore, produced hormonal symptoms.

The distinct difference in prognosis noted between the renal celled and the transitional celled groups of tumors is challenging. Were it possible to say that the former were derived from the mesodermal metanephric "cap" and the latter from the entoderm, the answer would be simpler. The fact of the matter is that both metanephric cap and metanephric diverticulum are derived from mesoderm; the former comes from a more cephalically situated portion of the intermediate mesoderm, while the latter buds off from the mesonephric duct which, in turn, derives from more caudally situated elements of the same primordium. Another riddle that constitutes a corollary to this is the fact that the adult lining of the calyces, ureters and urinary bladder is the same throughout, although the bladder is largely derived from the entodermal urogenital sinus while the other structures are of mesodermal origin. Furthermore, during inflammation of a prolonged type, all these segments may undergo metaplasia and neoplasia of an identical sort. Perhaps too much stress has been laid upon the specificity of the primary germinal layers.

TABLE 2. *Incidence of pathologic types of renal tumors, 115 cases*

PATHOLOGIC TYPE	TOTAL CASES	PER CENT OF EACH TYPE
Total cases	115	100.0
I. 1. Adenoma	0	0.0
2. Renal celled carcinoma	74	64.5
II. 1. Transitional papilloma	2	1.7
2. Transitional carcinoma	13	11.3
III. 1. Embryonal carcinoma including Wilms' tumor	20	17.3
IV. 1. Extrarenal tumor	6	5.2

CLINICAL CORRELATION

Using the classification just discussed, we surveyed the 115 cases of renal tumors from the Memorial and New York Hospitals (table 2). Though the incidence of embryonal tumors may be disproportionally high, owing to the relatively large number of instances at the Memorial Hospital, the total series from that institution is otherwise comparable with that from New York Hospital, in that renal celled tumors are more common.

In order to evaluate the prognosis of renal tumors under this pathologic classification, all cases subjected to nephrectomy prior to 1943 were surveyed (table 3), as these would permit a determination of prognosis on the basis of five year postoperative survival. In this series there were 77 cases, 4 of which showed evidence of metastasis prior to operation. The remainder were subjected to surgery with hope of cure, as there were no proven metastases prior to operation, though in some the tumor had been known to exist for a considerable time. Cases classified as "indeterminate" are those which died within 5 years of other causes and without recurrence of cancer, and those lost to follow-up within the same period without evidence of recurrent disease. The calculations are based upon the determinate group only. From the standpoint of the pathologist's prognosis, it is unfair to consider deaths from the immediate effects of nephrectomy together with those attributable to recurrent cancer, although clinically they are both mortalities in the course of treatment for cancer. Similarly, the inclusion of cases with preoperative evidence of metastasis and admittedly less chance of survival offers another element of error in prognosis. Despite this, we considered these patients as "determinate" in our tabulation, feeling that the clinical standards should be maintained.

TABLE 3. *Five year postoperative survival in relation to pathologic type of renal tumor, 77 cases*

PATHOLOGIC TYPE	TOTAL CASES	INDETERMINATE	DIED UNDER 5 YEARS	LIVING 5 YEARS POSTOPERATIVELY	PER CENT 5 YEAR SURVIVAL
Total	77	13	41	23	35
I. 1. Adenoma	0	0	0	0	0
2. Renal cell carcinoma	47	10	22	15	41
II. 1. Transitional papilloma	2	0	0	2	100
2. Transitional carcinoma	11	1	9	1	10
III. 1. Embryonal carcinoma including Wilms' tumor	13	2	8	3	25
IV. 1. Extrarenal tumor	4	0	2	2	50

The 5 year survival of cases of renal celled carcinoma was 41 per cent. Four of the determinate cases showed the tubular variety of renal celled carcinoma, with a survival comparable to that of the group as a whole. The 37 determinate cases included 3 postoperative deaths and 4 patients on whom nephrectomy was performed after metastasis had occurred. Among these, 1 patient had a craniotomy for supposed primary cerebral tumor and subsequently a nephrectomy after the diagnosis had been pathologically established; he died 4 years later of cerebellar recurrence.

In both cases of transitional papilloma, the patients were alive and well at the end of 5 years, whereas in only 1 of the 10 determinate cases of transitional carcinoma did the patient survive 5 years. In 3 of these the subtype was epidermoid carcinoma and none survived 6 months. There was 1 postoperative death in this series.

There were 3 five year survivals in the group of 12 determinate cases of embryonal tumors, a rate of 25 per cent. Though the majority of patients died under 2 years after operation, 1 is still living 11 years after nephrectomy, while 2 died 9 and 10 years respectively after operation.

The extrinsic group included 2 leiomyosarcomas, 1 "sarcoma," and 1 rhabdomyosarcoma. While the patients with leiomyosarcoma survived 5 years, the other two died respectively one and 26 months postoperatively.

The life expectancy after 5 years in the renal celled carcinoma group is summarized graphically (fig. 4); for this 17 determinate cases subjected to nephrectomy prior to 10 years have been used; in addition, the survival of the 37 determinate 5-year cases has been plotted. Though the former group includes all the latter and the latter includes some of the former, a parallelism is noted which, if not of statistical value, does at least denote a significant trend.

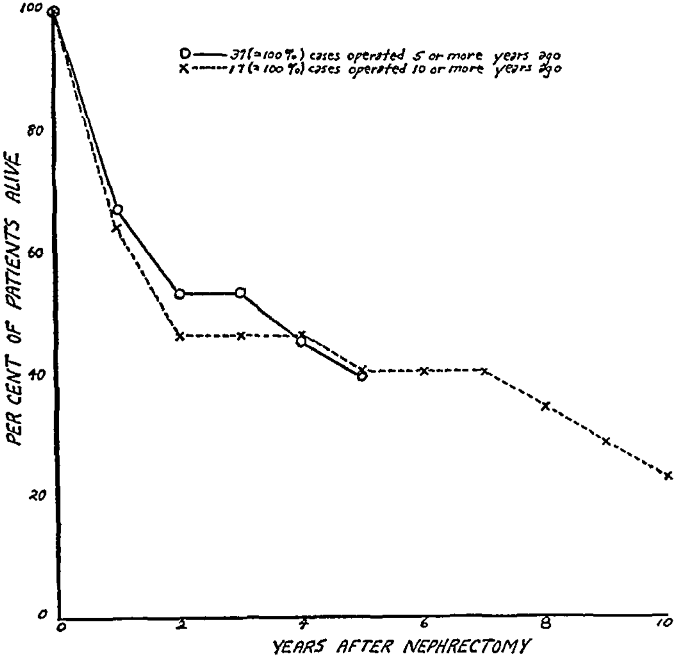


FIG. 4. Survival of patients with renal-celled carcinoma after nephrectomy

DISCUSSION

The difference in prognosis between the renal celled and transitional celled carcinomas has no histogenetic basis as we have previously observed. There is variation among the different types of renal celled carcinoma in regard to prognosis. Those showing a tendency to form tubules and papillae with numerous mitoses and extensive metaplasia offer just as poor a prognosis for five year survival as do the transitional or embryonal groups. Renal celled carcinoma growing in solid cords with isometric components and heavy trabeculae offer the best prognosis. In studying the sections obtained from the Memorial Hospital, without any knowledge of the case histories, an accurate prognosis for 5 year survival was forecast in over 90 per cent of the cases, as checked by subsequent comparison with the clinical records. The most frequent error was occasioned by the survival of a case just beyond the 5 year period, when the patient should theoretically have died within that span. The paucity of cases of transitional celled carcinoma and embryonal carcinoma permitted no opportunity for obtaining microscopic criteria as to why an occasional case survived. In general, the prognosis is poor for all of them. The 2 patients with leiomyosarcoma (in the group of extrarenal tumors) survived 5 years, apparently paralleling the expectancy in the case of similar tumors arising in the uterus.

CONCLUSION

A pathologic classification of renal tumors based upon histogenetic and histologic criteria is offered. It permits a constant parallel between groups of tumors and the prognosis following nephrectomy for ablation of the neoplasm.

The authors wish to express their appreciation to Doctor Fred W. Stewart, director of the Department of Pathology, Memorial Hospital, New York, N. Y., without whose kind cooperation this study would not have been possible.

REFERENCES

Foot, N. C. and Humphreys, G. A. The importance of accurate pathologic classification in the prognosis of renal tumors. Surgery, 23: 369, 1948.

Patten, B. M.: Human Embryology. Philadelphia and Toronto: The Blakiston Co., pages 556–561, 1947

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

DISCUSSION

MR. HENRY MORTENSEN (Melbourne, Australia): I should like to take this opportunity to thank your President and the executives of the Association for permitting me to be present at this meeting and asking me to enter into your discussion. I honor those privileges very greatly.

As we have long been aware, we have attempted to evaluate the prognosis in this serious disease of renal tumors in various ways and from various angles. We could say, broadly, that the approach to the problem was either microscopic or macroscopic, clinical or histological.

By far the greatest amount of research, mainly from a statistical point of view, has been done from a clinical or macroscopic aspect.

We remember the excellent paper of some two or three years ago by Melicow, who, as well as discussing the problem from a histological standpoint, endeavored to assess the prognosis in renal tumors from three points of view:

Firstly, the clinical history, where he pointed out that the patient who came in with a long history, with the story of a mass or lump rather than hematuria, presented a bad outlook.

Secondly, from the point of view of objective findings, where, of course, the patient with a fixed, hard mass, fever, and obliteration of pelvic filling in the pyelogram presents a poor prognosis.

Thirdly, from the condition of affairs at operation, namely, the larger the tumor, the graver the outlook; the question of involvement of renal vein; the question of the size of blood vessels, and the question of damage to capsule, or damage to blood vessels in the removal of the kidney.

McDonald and Priestley have also drawn attention to size of the tumor and involvement of renal vein as important elements in the paucity of the outlook; but we know also that these tumors are notoriously capricious. I am referring mainly to the cortical type, because I think it is generally accepted that the embryonal type, and the tumors of the collecting portion of the urinary tract, the upper urinary tract, provide a decidedly bad outlook from any point of view; whereas those of the cortical type may provide a more hopeful aspect, and concerning them especially we wish to evaluate that particular outlook.

The capriciousness of these tumors destroys the value of a lot of statistics with which we have been presented. We have all, I am sure, had the experience of removing, almost tearing out, a very large tumor, with spilling of tumor contents often into the wound, and have had the experience of seeing that patient living years afterwards; and, in contradistinction to that, we have all removed a tumor of five, six, or seven centimeters in diameter, perfectly encapsulated, feeling that here we have done a good job and have saved the patient, and have had the unhappy experience of seeing that patient return with metastases in a very short time.

I personally have seen a patient with a pathological fracture of the humerus arising from a secondary growth from a renal carcinoma where the original renal carcinoma was only two centimeters in diameter. We have, therefore, the unique possibility in a renal tumor of the metastasis being a solitary one. We have again the possibility, partly a probability, that removal of the primary growth and the metastases may produce a cure of the condition; in that state of affairs, the pathology is an extremely rare one.

One feels, sometimes, with these anomalies, that a cancer cell, particularly with renal tumor, reacts differently in different individuals, an aspect of malignancy not considered often enough; that is, just as an individual bacterium may produce a different reaction in different individuals, so the same cancer cell may react differently from the point of view of production of tumor and from the point of view of outlook, and, if that be so, God help us in endeavoring to evaluate prognosis!

So we see that the clinical side of progress is notoriously difficult, and are forced again to the histological point of view through an endeavor to get some help in this problem. One of the first to stress the importance of this aspect in malignancy was Broders, who, many years ago—over 25 years ago—taught us that the more highly differentiated the cells in a tumor, the less malignant it is and, in contradistinction to that, the less differentiated they are, the more malignant they are. This theory has proven most helpful through the years.

I am pleased that in this paper to which we have just listened, the term "hypernephroma" has been deleted from the classification. I feel that the use of that term has for many years prevented and precluded progress in the understanding of the tumors which we encounter in the renal cortex. Particularly it has produced a tremendous amount of difficulty in the minds of students who have been endeavoring to learn and understand something about this serious disease.

Lastly, I have only one criticism to make of the paper which we have just heard, and this I make with a certain amount of temerity. That perhaps is a minute fault, but in the classification of which we have seen but one portion, there is a reference to a "well-differentiated, nonmalignant, transitional papilloma,"—that of the collecting portions of the upper urinary tract.

From a histological point of view, I admit that the particular lesion which is described may appear to be perfectly innocent in its structure but we, I think, as urologists, have learned that there is no such thing as a nonmalignant papilloma of the collecting portion of the urinary tract. Having malignant tendencies, from the point of view of treatment it should always be so considered, and I would respectfully suggest that the term "nonmalignant" be deleted from the classification.

DR. JOHN HARTWELL HARRISON (Boston, Mass.): I asked to discuss this excellent presentation for several reasons. The last time that I had the pleasure of seeing Dr. Humphreys he was speaking at a surgical meeting in the Netherlands East Indies just 3 years ago. The contrast of surroundings then and now is too great to mention but the discussion of a very different subject today has been equally enjoyed by all of you. In addition I am afforded by your courtesy the opportunity of paying my respects to Mr. Mortensen to whom many Americans are indebted for his kindness and hospitality during the years of World War II.

In this so-called "schizoid atomic" era, it is appropriate that we pause and pay tribute to surgical pathologists who are still morphologists, histologists, biologists and yet may of necessity have to become physicists also in the future. There is a dangerous trend in medical education today which neglects the proper emphasis on the importance of a knowledge of pathology. Let us as surgeons acknowledge and remember our dependence upon the pathologist and our understanding of his teaching in order that we may gain stability and the possibility of prognostication in each individual neoplasm. Drs. Foot, Humphreys and Whitmore have presented a dependable classification of renal tumors and have correlated the histologic picture of each with the subsequent clinical behavior in order to establish a prognosis. The latter may be greatly improved if we educate the public and fully utilize all of our diagnostic facilities to accomplish an earlier discovery of neoplasm of the urinary tract.

(Slides were shown illustrating pyelograms and gross and microscopic pathology of cystic renal adenocarcinoma and papillary carcinoma of the renal pelvis and bladder as well as Papanicolaou stains of the urinary sediment.)

I should like to thank Drs. Foot, Humphreys, and Whitmore for their presentation to us and to tell Mr. Mortensen that I hope we can show to him something of our appreciation of his hospitality in Australia in the dark days of 1942.

DR. GUSTAVUS A. HUMPHREYS (New York, N. Y.): Mr. Mortensen brought out the fact that the papilloma might be theoretically deleted from the classification. I wish that were possible and, of course, clinically we have to operate on them all, even though our hindsight may prove that these lesions are benign.

These 2 patients have lived approximately 7 and 10 years respectively. The microscopic sections viewed by all the pathologists show these transitional papillomas are perfectly benign, and I think we are forced to admit that there are just 2 in 115 cases. It may occur rarely, so we just leave room for it in the classification but don't ever expect to see it again.

As to the classification, I am sorry I had to hurry in presenting it. It is much simpler than it appeared, presented in haste, and one of the reasons why I am fond of it personally is that it is a simple one that I can understand, whereas all the other classifications are extremely complicated and I can't correlate them in my mind.

The prognostic value of this classification, working in association with pathologists, gives us something in common to talk to the pathologist about, and is really most helpful. All I can say is that we have found it helpful to use this classification and the pathologist has been able to tell us, with uncanny accuracy, the prognosis of these tumors. I hope you will have the same experience when you use this classification.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

THE TREATMENT AND PROGNOSIS OF PAPILLARY TUMORS OF THE RENAL PELVIS AND URETER[1]

VINCENT J. O'CONOR

A complete survey of a large series of patients who have been subjected to nephrectomy in various clinics for cortical (solid) renal tumors suggests that little real progress as to prolongation of life has been accomplished by modern surgery. The operative mortality has been reduced to a minimum by most surgeons; yet earlier diagnosis and earlier nephrectomy has done little to secure an actual cure in most patients. Irradiation, except in the mixed tumors (Wilms') in infants, has been of no permanent help.

In contrast, the prognosis in papillary tumors of the renal pelvis and ureter has been spectacularly improved by earlier diagnosis and the application of complete nephro-ureterectomy.

A number of recent publications have described the "successful" local extirpation of a so-called "benign" papillary tumor of the ureter. This has always been done in the presence of a normally functioning opposite kidney. We do not believe that any papillary tumor of the renal pelvis or ureter, except the rarely encountered simple vascular polyp, can be considered as anything but potentially malignant.

The purpose of this paper is to attempt a fair evaluation of our own experience in this regard and to suggest that we should not lightly revert to incomplete surgery or surgical "stunts" in the treatment of the only upper urinary tract neoplastic lesion which has been so frequently cured by more radical surgery.

Vest has reported 3 cases of primary papilloma of the ureter, 2 sessile and 1 a pedunculated polypoid growth. Instead of routine nephro-ureterectomy the local tumor and surrounding ureteral wall were excised so as to preserve the kidney. Vest believes that on the basis of preoperative, operative, and postoperative findings, these particular tumors can be considered benign. A very considerable amount of statistical work has been done by many surgeons and pathologists with the conclusion that practically all ureteral tumors are malignant in character and that rarely can the degree of cellular malignancy of any given tumor in the renal pelvis or ureter be determined by preoperative examination. Vest contends that "benign" tumors occur as epithelial growths showing no histological evidence of malignancy or as polyps made up of benign stroma with a transitional epithelial covering. Ottley says that "benign papilloma of the ureter" is a rare condition. She, in her search of the literature, brought to light only 27 instances in which the diagnosis was confirmed by inspection of the interior of the renal pelvis and ureter together with microscopic examination of the tumor. Papillary pelvic tumors tend to grow slowly. The "relatively benign" growths, according to Ottley, occurred in the younger age groups (third decade). Some of these tumors grew along the ureter and into the bladder. In a number of cases the tendency to subsequent development of papillary neoplasms in the ureter, bladder, and urethra suggested the existence of a neoplastogenic proclivity of the entire urothelium. The rarity of primary ureteral tumors appears to be a mere conception passed on by most authors who report a single or an occasional instance.

---

[1] Read at annual meeting, American Association of Genito-Urinary Surgeons, Skytop, Pa., May 12-14, 1948.

Jaffe and Mendillo state that primary carcinoma of the ureter in their experience is relatively rare. They found only 2 cases among 90,000 routine admissions to Grace Hospital, New Haven, Connecticut. Of these 1,900 admissions were for primary malignancy in various body locations. However, since two-thirds of the reported cases of primary carcinoma of the ureter have appeared in the literature during the past 10 years, it would seem that this lesion is being diagnosed and treated more frequently than in the past. These authors stress the fact that total nephro-ureterectomy with removal of a cuff of bladder and of the perirenal and peri-ureteral fat is the ideal treatment.

Counseller, Cook and Seefeld followed 18 cases of primary epithelioma of the ureter and added 9 new cases. The grade of tumor in their experience was the main factor influencing prognosis. They emphasize that complete nephro-ureterectomy with removal of a cuff of bladder should be done in every instance.

Bothe states that an analysis of the etiologic factors has shown a lack of clear understanding of the mechanism involved in carcinoma of the renal pelvis and ureters. Six surgical specimens were studied by him and the early changes in the subepithelial supporting tissue was inflammatory in type in all instances. This reaction was followed by proliferation of the basal layer which eventually became papillary or infiltrating. Bothe gives the vague but generally accepted idea that there must be some irritant to the ureteral epithelium by a carcinogenic agent either local, blood-borne or lymph-borne. Fagerstrom has recently presented a valuable paper on the relationship of epithelial crypts, buds and nests. Microscopic investigation of the ureters removed from 120 autopsies was carried out in order to study epithelial aberrancies in their incipient stage, and to determine, if possible, their etiologic significance in solid and cystic tumors of the ureteral mucosa. Six clinical patients, presenting various types of mucosal neoplasms, were discussed by Fagerstrom and the microscopic findings in surgical specimens were correlated with the epithelial changes found in the autopsy series. Fagerstrom concludes that hyperplasia of the urinary epithelium may result from local irritation, such as chronic infection or more noxious agents circulating in the body fluids. Epithelial buds and crypts are but bizarre expressions of epithelial hyperplasia, according to Fagerstrom. The theory of "cell nest" formation, as proposed by von Brunn and accepted by most writers, is not supported by Fagerstrom's study. Cystic tumors of the ureteral epithelium are derived from occluded mucosal crypts, whose cell lining exercise a latent secretory potentiality. Fagerstrom was unable to develop any evidence that solid epithelial buds are directly associated with the origin of solid tumors of the urinary epithelium.

In view of the present lack of definite knowledge as to the etiology of papillary carcinoma of the renal pelvis or ureter, aside from the fact that these lesions are

A second similar case is living and well 4 years after ureterectomy and coagulation of multiple papillomas in the bladder. It is 7 years since the original and incomplete operation.

CONCLUSIONS

The treatment of choice, in dealing with papillary tumors arising primarily in the renal pelvis or ureter, is complete nephro-ureterectomy.

Incomplete ureterectomy is very often followed by recurrence, or subsequent tumor development, in the ureteral stump, intramural portion of ureter, or in the bladder mucosa.

These secondary tumors are usually more extensive than the primary lesion and as a rule are less amenable to destruction.

Papillary tumors of the upper urinary tract are often associated with stone and chronic infection. Microscopic study of many of the ureters which have been removed from these patients suggests a widespread or diffuse metaplastic response to an apparent carcinogenic agent on the part of the ureteral epithelium.

In the light of these findings, it seems that we are hardly justified in ever making the diagnosis of a "benign" papillary tumor of the renal pelvis or ureter.

To recommend local excision of ureteral tumors would seem a step backward in the treatment of the only neoplastic condition of the upper urinary tract in which, by complete surgery, we have improved the end results and period of postoperative survival.

55 E. Washington St., Chicago, Ill.

REFERENCES

Bothe, A. E.: J. Urol., 49: 69–76, 1943.
Counseller, V. S., Cook, E. N. and Seefeld, P. H.: J. Urol., 51: 606–615, 1944.
Fagerstrom, D. P.: J. Urol., 59: 333–358, 1948.
Ferris, D. O. and Daut, R. V.: J. Urol., 59: 577–579, 1948.
Jaffe, S. A. and Mendillo, A. J.: Am. J. Surg., 62: 126–133, 1943.
Ottley, C. M.: Brit. J. Surg., 32: 531, 1945.
Vest, S. A.: J. Urol., 53: 97–121, 1945.

The Journal of Urology
Vol 61 No 3 March 1949
Printed in U S A

TUMORS OF THE URETER[1]

FRANK COLEMAN HAMM AND LAWRENCE L LAVALLE
From the Department of Urology of The Brooklyn Hospital, Brooklyn, N Y

Six cases of ureteral tumor have been observed at The Brooklyn Hospital The first case, reported by Rathbun, involved metastatic tumor secondary to a carcinoma of the breast which was discovered in a 58 year old man who had undergone a mastectomy 3 years previously Microscopic examination of the tissue obtained from a nephro ureterectomy revealed adenocarcinomatous structure which was indistinguishable from sections of tissue obtained at the time of the mastectomy, and diagnosed as mammary carcinoma About 5 years later, he died of generalized carcinomatosis

The second case was that of C S , a 68 year old man who was seen by us on June 9, 1939, for the first time His symptoms had been studied, and a diagnosis rendered by a competent urologist whose records were not available to us However, the clinical course seemed to confirm his diagnosis Treatment had included a nephrostomy elsewhere, and the man refused further surgery After having lived in comfort for 2 years, he died of generalized carcinomatosis

The 4 cases which form the basis of this report proved to be primary ureteral tumors varying in character from a benign polyp to a very malignant papillary carcinoma (fig 1) These cases were diagnosed clinically In a review of 2, 407 reports of autopsies, no record of ureteral tumor was found

It is difficult to arrive at an accurate figure for the total number of ureteral tumors reported but the number does not appear to exceed 180 Doubtless many cases were either undiscovered or not reported Among those cases appearing in the literature, there is confusion as to which actually originated in the ureter While several instances of ureteral tumor were noted as findings at autopsy, it was not until early in the twentieth century that Albarran made a correct preoperative diagnosis Since that time, many excellent and comprehensive case reports and reviews have been written, including those by Cook and Counseller, Foord and Ferrier Higgins, Jaffe and Mendillo, Kretschmer, McCrea, Morse, Scholl and Gallagher, and Scott Refinements in diagnostic methods and an increased awareness of the possible occurrence of these tumors on the part of clinicians, as well as lower mortality rates in the age group over 50 years, should greatly expand the number of cases reported

CASE REPORTS

Case 1 On May 26, 1946, a woman of 20, in her second month of gestation, was admitted to the hospital complaining of acute pain in the right lower abdominal quadrant of 5 hours' duration, it was colicky in character The urine contained a moderate number of leukocytes and many red blood cells A tentative diagnosis of ureteral calculus was made The following morning cystoscopy,

---

[1] Read at annual meeting, American Association of Genito Urinary Surgeons, Skytop, Pa , May 12, 1948

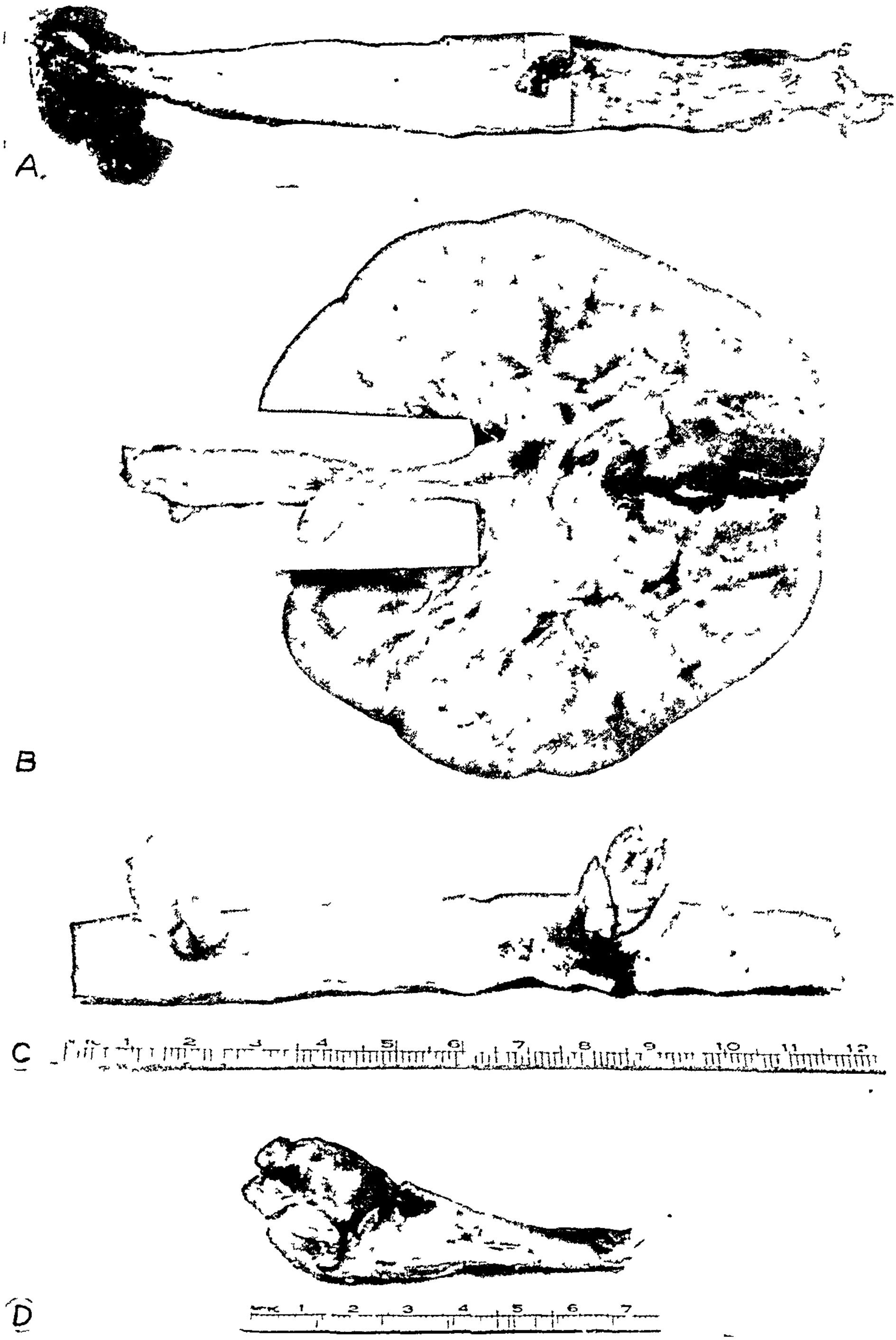


FIG. 1 Gross specimens of ureteral tumors *A*, case 1 A small polypoid tumor with a slender attachment is situated in lower segment of ureter, upper portion of ureter having been previously resected along with kidney *B*, case 2 In upper end of ureter is an ovoid papillary tumor with a very slender pedicle *C*, case 3 Two papillary tumors of unusual structural appearance lay in lower ureter When ureter was incised, both were found hanging downward toward bladder. *D*, case 4 Lower ureteral segment widened by an intraluminal mass with a broad area of attachment

under pentothal anesthesia, was performed. A papillomatous mass was seen protruding from the right ureteral orifice and was excised (fig. 2). A retrograde pyelogram was made. Our pathologist, Dr. J. Arnold deVeer, reported the specimen as a branching polypoid mass of seminecrotic tissue containing old and recent hemorrhage. Within several lymphatic channels there were collections of cells suggesting extensions from a malignant epithelial tumor (fig. 3, *A*).

The roentgenograms indicated the presence of an obstructing lesion of the right lower ureter, with hydroureter and hydronephrosis (fig. 4). The opposite kidney and ureter showed good filling and the dye appeared within the normal time. A diagnosis was made of a nonfunctioning right kidney resulting from a ureteral tumor. One week after admission, the patient began to experience lower midline abdominal pain and an abortion occurred within a short time. When surgical intervention was decided upon, a 2-stage procedure was chosen in view of the fact that there had been a recent spontaneous abortion and that the patient was not particularly robust. On June 7, as a first stage, nephrectomy and a partial ureterectomy were performed. The second stage was undertaken on June 25. At that time, the upper end of the ureter had to be dissected free of adhesions that had followed the first operation. The remainder of the ureter was resected along with a cuff of bladder about 2 cm. in diameter. The bladder defect was closed with interrupted chromic sutures and a Penrose drain placed at the site. Bladder drainage was provided by a No. 20 Foley catheter in the urethra.

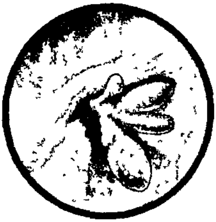


FIG. 2. Case 1. Artist's representation, based on authors' description, of a papillomatous mass observed cystoscopically at right ureteral orifice.

In the laboratory, the distal portion of the ureter was found to measure 15 cm. in length. Six centimeters from its proximal end, the lumen was occupied by a slender, ovoid, brown, polypoid mass 2 cm. in length attached by a narrow pedicle to the mucosa (fig. 1, *A*). The site of attachment was not more than 3 mm. in diameter. The tumor was slightly lobulated, but its surface was generally smooth and shiny. Sections were made through the pedicle and long axis of the mass. The latter was found to be composed chiefly of edematous and hemorrhagic connective tissue. The surface was covered by an epithelial layer resembling that of the ureter. No evidence of malignant tumor could be found (fig. 3, *B*). A cuff of bladder mucosa resected with the ureter was shown to be edematous and inflamed but it, likewise, contained no neoplastic tissue structures. The kidney, on section, showed considerable damage from obstruction

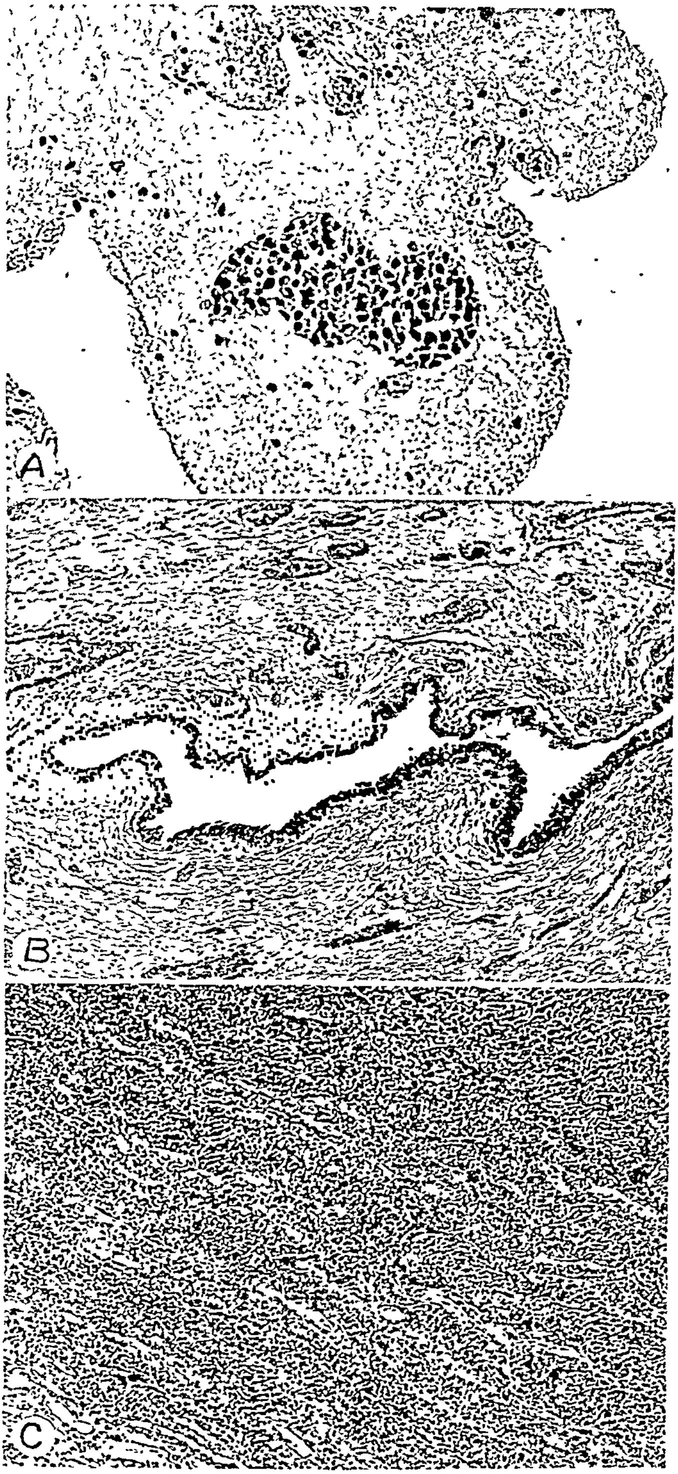


Fig. 3. Case 1. *A*, portion of polypoid tumor removed from right ureteral orifice. Mass is nonneoplastic, consisting of edematous, seminecrotic, connective tissue. No epithelial covering is shown. Space in center of field was originally interpreted as a lymphatic channel filled with tumor cells, but was later thought probably to represent a focus of ectopic decidual reaction. *B*, epithelial-lined space across center of field separates wall of ureter from polypoid mass within its lumen. Latter consisted of edematous hyperemic connective tissue. Epithelial covering is of adult character but has been somewhat eroded. No neoplastic features were found. *C*, portion of medulla of kidney showing acute cellular infiltration. Toward right and above, process is frankly suppurative. Toward lower left corner, diagonally placed tubules become more clearly visible.

and infection (fig. 3, *C*). Because the patient had been found to be pregnant and because no source of metastatic tumor could be discovered, it was decided that the cells found in the lymphatic channels of the polyp at the ureteral orifice represented not a malignant process but part of an ectopic decidual reaction. The subsequent operative findings and clinical course of the patient also discredited the idea that the cells in question were cancer cells.

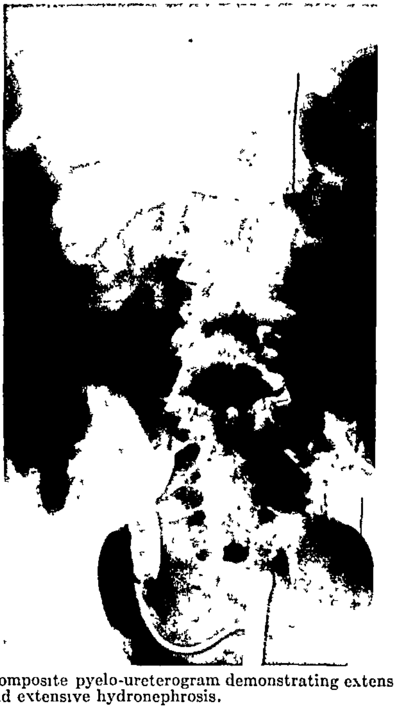


FIG. 4. case 1. Composite pyelo-ureterogram demonstrating extensive filling defect in lower right ureter and extensive hydronephrosis.

During her recovery, there was a mild elevation in temperature possibly caused by a low grade infection or a slight extravasation from the bladder. A small mass in the right lower abdominal quadrant was discovered which became smaller and disappeared. The woman left the hospital 8 weeks after admission in excellent condition. On August 26, 1946, the interior of the bladder was inspected and found to be free of tumor. In January 1947, she again became pregnant and was delivered spontaneously on October 18. An examination in May 1948 disclosed no evidence of tumor.

Case 2. A 59 year old woman was admitted to the hospital on April 15, 1946, Retrograde pyelograms revealed no conclusive cause of hematuria. The patient was short and heavily built so that the intravenous pyelograms did not provide good visualization. Because all bleeding had ceased, the patient requested discharge from the hospital; he was instructed to return in 3 months for further study.

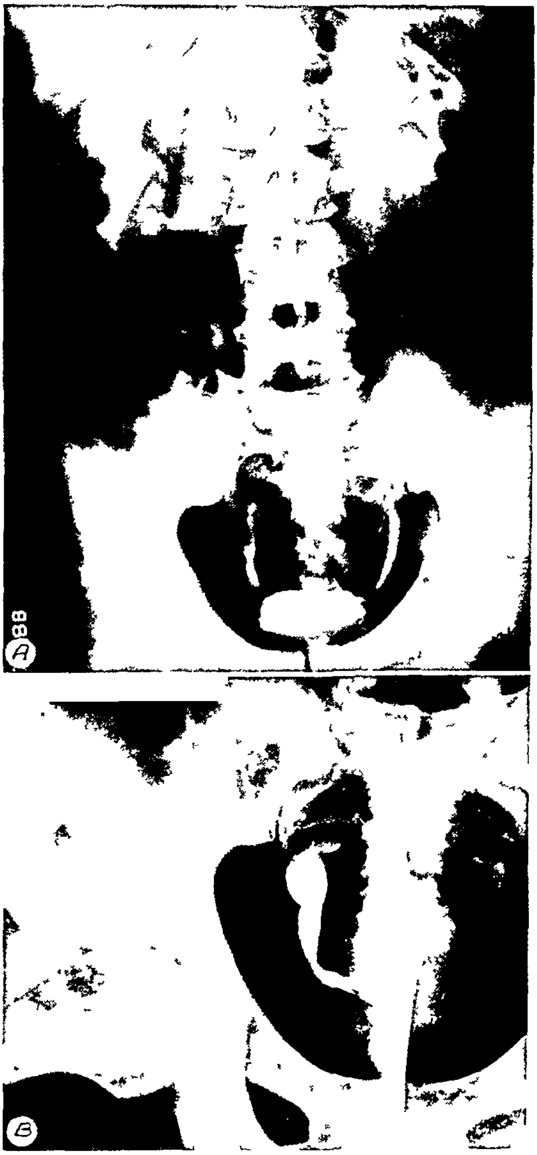


Fig 7 *A*, case 3. Filling defect in lower ureter with early hydronephrosis *B*, close-up view of right lower ureteral area.

No blood was seen in the urine for 4 months. At that time, he began to experience backache on the right side which interfered with his work. On January 9, 1948, he was re-admitted to the hospital with the chief complaint of backache of 4 weeks' duration. Cystoscopy revealed a normal bladder and normal ureteral orifices. The catheterized specimen of urine from the bladder as well as from both kidney pelves was clear. A hydronephrotic drip was noted from the right side. The retrograde pyelo-ureterograms definitely indicated the presence of a mass in the lumen of the lower right ureter (fig. 7). Five days later, a bulbous-tip catheter was passed into the right ureteral orifice and an air ureterogram was made which confirmed the previous findings of a right ureteral tumor. Study of the urinary sediment showed many flat cells, but no tumor cells or tissues.

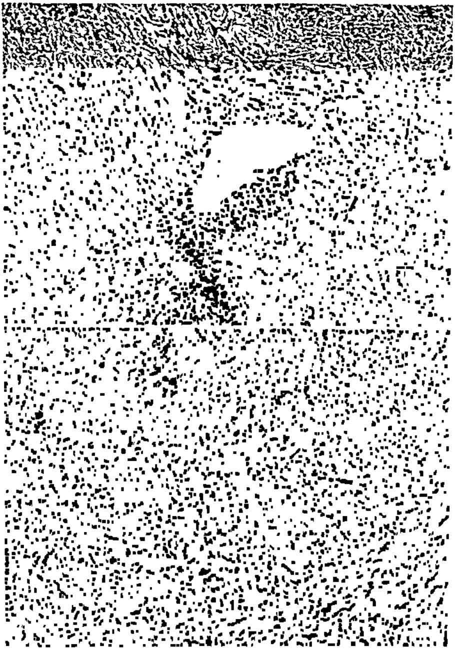


FIG. 8. case 3. *A*, portion of ureteral wall just beneath base of attachment of one of two papillary tumors (fig. 1, *C*). There is a small space partly lined by well differentiated tra [illegible] that is neither readily identifiabl [illegible] esent in the surrounding tissue. *B*, [illegible] ureteral wall at site of attachment of one of tumors.

On January 20, 1948, a right nephrectomy and partial ureterectomy were performed through the usual loin incision. The patient's condition being good, he was turned on his back and a midline incision was made from the umbilicus to the symphysis pubis. The ureter was readily separated from the peritoneal attachment and removed at the bladder. The resected portion of the ureter was 14 cm. in length, its wall was thickened and the lumen dilated. When opened by a longitudinal incision, two tumors of very similar size and appearance were found attached to the mucosa at points 6.5 cm. apart (fig. 1, *C*). Each tumor hung downward into the lumen, was 2 cm. in length and had a pedicle 2 mm. in diameter. The diameters of the tumors differed by a few millimeters, and each presented a papillated appearance. They were of friable texture and very pale, almost white. There was no gross evidence of invasion of the wall of the ureter.

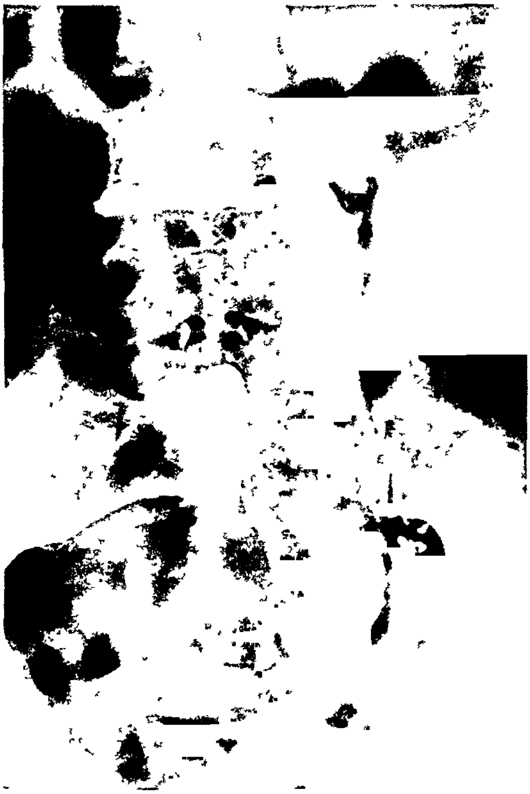


Fig. 9. Case 4. Ureterogram showing cup-shaped deformity indicating tumor in upper segment of ureteral stump, kidney having been previously removed elsewhere. (Contrast medium had been introduced into spinal canal at some earlier time.)

Microscopically the tumors presented almost identical structure. They were composed of long villous processes with slender, branching stalks and a covering of transitional epithelial tumor tissue. In the depths of the masses, there was a tendency for the villi to coalesce into solid sheets of tissue. Any irregularity in cell structure was slight. However, at the base of one of the tumors, there was evidence of invasion of the ureteral wall, focal anaplasia and squamous metaplasia accompanied by some focal inflammation (fig. 8). The other tumor appeared to grow outward without invasion or inflammation at its site of attachment. It was, therefore, reported that one of the ureteral tumors showed early focal malignant transformation. The small round nodule in the kidney proved to be a benign intracystic adenoma. The kidney was also the seat of mild, chronic pyelonephritis with hydrops of the pelvis.

Case 4. H. B., a 49 year old man, was seen first on August 24, 1944. At another hospital, he had undergone a nephrectomy on the right side for severe renal pain and hematuria 4 months previously. Pyelograms were reported to show extensive destruction of the kidney, but the ureteral tumor was not recognized. His mother had died of cancer, but the history was otherwise irrelevant.

At the time of admission to the hospital, a firm, tender mass was palpable in the right side of the abdomen and constant, severe lumbosacral pain which radiated to the right loin and right thigh was present. Cystoscopy was performed, and a ureterogram, made of the stump, revealed a cup-shaped deformity characteristic of tumor (fig. 9). On September 5, 1944, an abdominal exploration was carried out and a large, hard, retroperitoneal tumor was found. It was impossible to remove the entire mass due to its attachments to the ilium and vena cava. The ureter contained a bulb-like enlargement near the point where it had been severed at the previous operation. It was dissected down to the bladder and removed.

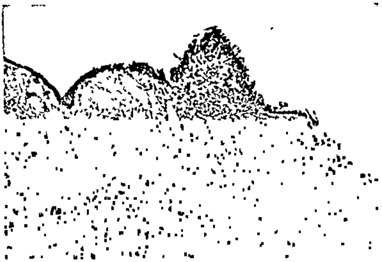


FIG. 10. Case 4. Section of wall of ureter Darkly-shaded area covering entire right half of specimen represents infiltration by tumor tissue Toward left border, clumps of tumor cells are seen in distended lymph channels.

Two specimens were submitted for pathologic examination; one was the resected segment of ureter and the other, a portion of the retroperitoneal tumor tissue. The lumen of the ureter was distended by a spheroid mass 1.5 cm. in average diameter. It was attached to the wall by a pedicle approximately 1 cm. in thickness and presented a papillomatous appearance suggesting massed villous structure (fig. 1, *D*). The specimen obtained from the retroperitoneal (metastatic) mass appeared to be fibrous tissue studded with small red-brown patches.

Microscopic examination showed the primary growth to be a villous papillary carcinoma of transitional type with considerable anaplasia. The tumor had invaded the wall of the ureter and was found in lymph channels and blood vessels within the wall. The retroperitoneal mass consisted largely of fibrous tissue, containing also many islands of carcinoma scattered throughout the tissue but lying chiefly within the lymph channels (fig. 10). The patient recovered from the operation and was discharged from the hospital in fair condition, but died within 6 months of generalized carcinomatosis.

DISCUSSION

There are no recognized signs and symptoms characteristic of ureteral tumor, although pain and hematuria are commonly associated with these cases. Palpation of a mass near the location of the tumor is a late sign, usually indicating a marked extension of the tumor to the surrounding structures. The kidney on the affected side may be enlarged from the ureteral obstruction.

Ureteral tumors occur more frequently in the sixth and seventh decades of life. The average age of patients reported in the literature was 55 years, the youngest being 20 and the oldest, 89. The ratio of men to women was about 2 to 1. The right ureter was involved more frequently than the left. In our series, the youngest patient was 22 years old.

Pain was present in all 4 cases, being fairly typical of renal and ureteral disturbances, and was caused apparently by urinary obstruction except in the fourth case, in which the pain was due to extensive local metastasis. Hematuria was present in all cases, being rather severe in 2 and mild in the other 2. The diagnosis in each instance was made at cystoscopy.

According to other investigators, 75 per cent of ureteral tumors occur in the lower third of the structure. They point out, too, that in approximately one-third of these cases, obtaining a biopsy specimen and assuring a correct diagnosis is a simple matter for the tumor protrudes from the ureteral orifice. In other instances, where the origin of pain or hematuria remains obscure, accurate visualization of the ureter is necessary, and the importance of repeated cystoscopic examinations is emphasized.

The ureteral epithelium is of mesodermal origin and the bladder epithelium is derived from endothelium. There is no line of demarcation between the two, and the epithelium from one is indistinguishable from the other. They give rise to essentially the same types of neoplasm. They are similar in microscopic and gross appearance, and run the same clinical course. For practical purposes, all tumors of the urinary tract should be regarded as malignant. The poor end results reported for ureteral tumors suggest that the degree of malignancy may be higher than that of bladder tumors. The papillary carcinomata exhibit a tendency to invade adjacent structures, and metastasis to regional and retropubic lymph nodes has occurred in 48.1 per cent of cases in the series reported. Metastasis to distant organs is the rule in advanced cases. Adenocarcinomas have been reported also and, as may be expected in connection with any obstructing lesion, urinary stone formation is frequently found.

From the structural viewpoint, ureteral tumors may be classified as: papillary; nonpapillary, or sessile; polypoid. The papillary type predominates and usually represents the less malignant variety of tumor. The sessile type is squamous in character and is usually associated with infiltration. Both of these varieties are derived from lining epithelial structures. The polypoid tumor is derived from the submucosal structures and is covered by normal epithelium continuous with the epithelium of the ureter. This type of lesion is illustrated in our first case. The other 3 cases represent papillary tumors; no instance of the sessile type was observed. Tumors may be multiple as illustrated in case 3.

TREATMENT

In view of their potentially malignant nature, treatment should consist of early and complete surgical removal. The choice of operation will vary with the character and location of the tumor, the status of the uninvolved kidney, and the general condition of the patient. The more radical procedures are preferred and, in instances where the patient's condition permits, complete nephrectomy, ureterectomy and excision of a cuff of the bladder should be done at the same time. Unnecessary opening of the ureter should be avoided. Whenever the unaffected kidney is thought to be insufficient to support life, various compromises will have to be made, such as resection of the ureter with anastomosis, ureterostomy, or nephrostomy. Resection of the mucous membrane of the ureter may be done in noninfiltrating growths. Stang and Hertzog noted that of 149 patients on whom operation was reported, 33 or 24 per cent died soon enough to be classed as operative deaths. Proper study of the patient with careful selection of the operative procedure should greatly reduce this hazard.

80 Hanson Place, Brooklyn 17, N. Y.

REFERENCES

ALBARRAN, J.: Epithelioma de la partie inférieure de l'uretère. Bull. et mém. Soc. de Chir. de Paris, 32: 669, 1906.
COOK, E. N. AND COUNSELLER, V. S.: Primary epithelioma of the ureter. J.A.M.A., 116: 122, 1941.
FOORD, A. G. AND FERRIER, P. A.: Primary carcinoma of the ureter. J. A. M. A., 112: 596, 1939.
HIGGINS, C. C.: Primary carcinoma of the ureter. Ann. Surg., 108: 271, 1938.
JAFFE, S. A. AND MENDILLO, A. J.: Primary carcinoma of the ureter. Am. J. Surg., 62: 126, 1943.
KRETSCHMER, H. L.: Primary carcinoma of the ureter. Surg., Gynec. & Obst., 38: 47, 1924.
MCCREA, L. E.: Primary carcinoma of the ureter. Urol. & Cutan. Rev., 46: 485, 1942.
MORSE, H. D.: Primary papillary epithelioma of the ureter. Canad. M. A. J., 15: 902, 1925.
RATHBUN, N. P.: Scirrhous carcinoma of ureter. Trans. Am. Assoc. Genito-Urin. Surg., 21: 373, 1928.
——: Personal communication.
SCHOLL, A. J. AND GALLAGHER, V. J.: Primary papillary carcinoma of the ureter. Calif. & West. Med., 57: 180, 1942.
SCOTT, W. W.: A review of primary carcinoma of the ureter. J. Urol., 50: 45, 1943.
STANG, H. M. AND HERTZOG, A. J.: Primary carcinoma of the ureter. J. Urol., 45: 519, 1941.

The Journal of Urology
Vol. 61, No. 3, March 1949
Printed in U.S.A.

CYSTIC URETEROVESICAL PROTRUSION: REPORT OF FOUR CASES IN CHILDREN AND TWO IN ADULTS[1]

HENRY O. MERTZ and (by invitation) JOHN W. HENDRICKS and ROBERT A. GARRETT

From the Department of Genito-Urinary Surgery, Indiana University School of Medicine, Indianapolis, Indiana

We wish to consider the problem of congenital cystic ureterovesical endings in contradistinction to the more common finding of ureterocele, in the following report, distinguishing the former from the latter primarily on the basis of absence of a demonstrable ureteral orifice in the cystic dilatation.

INCIDENCE

While this curious congenital deformity is not exceedingly rare, it is encountered infrequently enough to warrant a report of additional cases, as well as a résumé of the known facts concerning it to date.

Bostroem, in 1884, first called attention to this disease, demonstrating its existence in autopsy material. Regner, and Bottomley in 1910, were able to accumulate 23 such cases from the literature. Of these 21 were discovered at autopsy. Their reports, especially that of Bottomley, called attention to the high coincidence of ureteropelvic reduplication, existing in 15 of the 23 cited cases. Eisendrath, primarily reporting lesions of the upper ureter, described one such patient who ultimately came to nephrectomy. Muschat, in 1934, perhaps reports the first clinical history of cystic ending of a reduplicated ureter in a living individual. The cyst had reached such proportion that it not only blocked its fellow ureter and that of the opposite side, but also achieved ball valve blockage of the urethra. Uglew described a cystic ending, probably imperforate, in a reduplicated ureter of a one year old infant. He reported a return of renal function two weeks after excision of the cyst through a suprapubic cystotomy. Spooner and Lindsay add a single autopsy case in which ilio-cecal stenosis, imperforate anus, hare lip and cleft palate also were found. E. L. Young cites one clinical case in which the cyst was destroyed without subsequent return of renal function. Seven years later nephrectomy was performed, demonstrating ureteropelvic reduplication as well as renal hypoplasia. Sargent published an account of a single case of cystic ureteral ending, again associated with ureteropelvic obstruction. In an excellent presentation of the problem, Dourmashkin adds another such case in which he demonstrated microscopically the presence of an opening undetectable by cystoscopic examination. With such a finding, he questions whether such a true cystic deformity actually exists. Michon reported a single case of reduplication in the presence of cystic ureteral ending.

Adding 6 clinical cases of our own to those found in the literature, the total number is found to be 38. In consideration of the coincidence of ureteral reduplication, this lesion existed in 25 (65 per cent) of the 38 collected cases, and in 4 of 6 of our own series.

---

[1] Read at annual meeting, American Association of Genito-Urinary Surgeons, Skytop, Pa., May 14, 1948.

ETIOLOGY

While cystic endings, and parenthetically ureteroceles, are assumed to be congenital in origin by most writers, Young conjectures an acquired mode of pathogenesis. However, Chwalle in 1927, recapitulating the embryogenesis of the ureter, reported a variation in the normal ureterogenesis as observed in a 28 mm. embryo. In exhaustive studies of the ureterovesical juncture morphogenesis he noted that there normally exists a ureteral membrane which occludes and precedes the patent ureteral meatus This membrane shatters in the normal development from a 12 to 28 mm embryo, the fragments sloughing, leaving the unobstructed ureteral orifice. Should mesenchymal tissue invade the space between the ureteral and vesical epithelium, shattering may not take place, giving rise to a blind uretero-vesical ending

TABLE 1

FINDING	INCIDENCE
Pyuria . .	6
Sepsis	4
Dysuria	3
Urinary difficulty	2
Flank pain	2
Urinary frequency	2
Mass in flank .	1

DIAGNOSIS

Diagnosis may be difficult, especially inasmuch as these lesions usually manifest themselves in the very young. The picture is predominantly one of urosepsis. In table 1 are listed the outstanding clinical findings in their order of frequency in our series.

Ultimate resolution of the diagnostic problem lies in the cystoscopic detection of the intravesical protrusion which may be visualized in the supplementary cystographic studies as a filling defect.

At cystoscopy a cystic mass was found in each of our patients, situated in the region of the involved ureter. In 3 of our series, the cysts were of massive proportions, occupying the greater part of the bladder. In 1933 one of us (H. O. M.) devised a method of diagnosis in these cases, which we have been unable to find duplicated in the literature. The shaft of a No. 23 hypodermic needle, having been severed from its shank, was inserted into a No. 4 ureteral catheter, whose catheterizing tip had been cut away. The needle was tied firmly in place with silk and then sealed with beeswax (fig. 1). Passing this catheter with the needle in place through the cystoscope, the ureterovesical cysts were then pierced, their contents aspirated and radiopaque material was injected. It was in this manner that we have arrived at a final diagnosis in 4 of our 6 cases. Contrast roentgenography in these 4 cases visualized the cystic endings and disclosed tortuous hydroureters. However, the pelvic systems were never completely filled in any patient due to the injection of insufficient pyelographic medium. Intravenous urography was of help for the most part in the determination of the presence or absence of functional renal tissue.

CASE REPORTS

Case 1. E. H. (M.H. 2115-55032) aged 42, a white woman, was admitted to the hospital on March 23, 1933 for removal of uterine fibroids. She had complained of left flank pain intermittently since its inception 9 months prior to admission. It was her impression that an episode of urinary difficulty had initiated the flank pain and had recurred with each repeated attack.

A general physical examination was not remarkable aside from the findings of of uterine enlargement. The temperature was 99.2 F. and the blood pressure was 120/100.

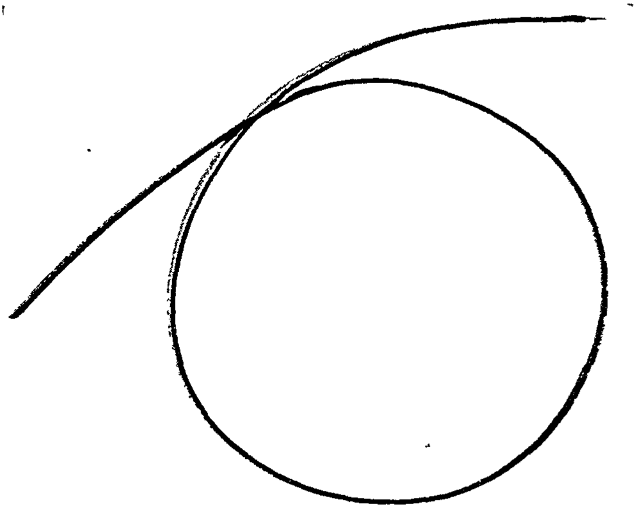


FIG. 1. Ureteral catheter with needle tip enabling puncture of cystic protrusion, evacuation of its contents and injection with skiodan.

Urinalysis showed acid reaction, 1.008 specific gravity, trace of albumin, loaded pus cells, red cells and bacteria. The blood count was not remarkable. A phenolsulphonphthalein test indicated 57 per cent excretion in the first hour. Both E. coli and staphylococci were isolated in culture.

Cystoscopic examination, performed on the day of admission, disclosed a large cystic-like bulging from the left bladder floor upon the superior surface of which a crescentic ureteral orifice was detected and catheterized, with no effect on the appearance of the cyst. Using the needle-tipped ureteral catheter the cystic mass was then pierced and 20 cc of turbid urine aspirated. A normal right ureteral orifice was identified and catheterized. Analysis of the three specimens thus obtained revealed many pus cells in the fluid from the mass, and normal findings in the other two. With the catheters thus oriented, retrograde pyelography was executed. A normal right pyelo-ureterogram was present; a left caudal pyelogram indicated mild hydronephrosis whereas the pelvic system injected through the needle was found widely dilated, incompletely filled, and associated with a tortuous hydro-ureter (fig. 2).

With a Stern-McCarthy resectoscope the cystic mass was unroofed, a cloudy outpouring of its contents immediately obscuring the visual field After repeated washings the cephalic ureteral orifice was visualized and found to be undisturbed.

The patient did well for several weeks on bladder catheter drainage, until April 15 when sharp right flank pain occasioned repeated cystoscopy. Two easily catheterized left ureteral orifices, the more caudal being the neo-ostium fashioned by electrocautery, were found. No cause for right flank pain could be demonstrated, the urine from the right kidney and the left caudal pelvis again being clear. Pyuria persisted from the left cephalic pelvis. The patient was discharged May 13.

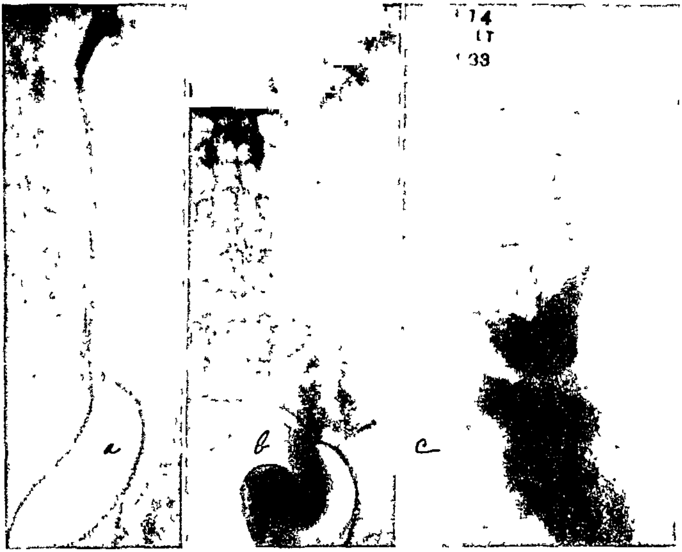


FIG. 2. Case 1. Ureteropyelogram of double left kidney b and c, Visualization of cephalic pelvis and its ureter after penetration of cyst and injection of skiodan. b, Antero-posterior, c, lateral position

Subsequent follow-up visits have indicated persistence of moderate pyuria, the right kidney continuing free of infection. No pain or febrile episodes have occurred since discharage. Excretory urography on January 29, 1939 indicated good function on the right with normal pelvic outline. The faintest pooling of dye was noted in the cephalic pelvis on the left side. This patient was last seen in December 1947 having no complaints.

Case 2. M. A. W. (XR 55787), a 7 month white girl was admitted to the hospital on November 19, 1941, having been referred because of acute otitis media. After clearing of the otitis, the infant continued to suffer febrile episodes, the temperature reaching 105 F. In addition the child seemed to cry with each micturitional act. For 2 months prior to admission the urine was known to be loaded with pus. The available urinary antiseptics had failed to alter the course of the infection.

Scarring of both tympanic membranes was the only significant finding. The temperature on admission was 101.4 F. Blood count showed 12.5 gm. of hemoglobin, 25,900 leucocytes of which 7 per cent were bands, 32 per cent were adult polymorphonuclears, 51 per cent were lymphocytes and 9 per cent were monocytes. Maternal Kline and Mazinni serologic reactions were negative. Urinalysis disclosed 1 plus albumin, acid reaction and loaded pus cells.

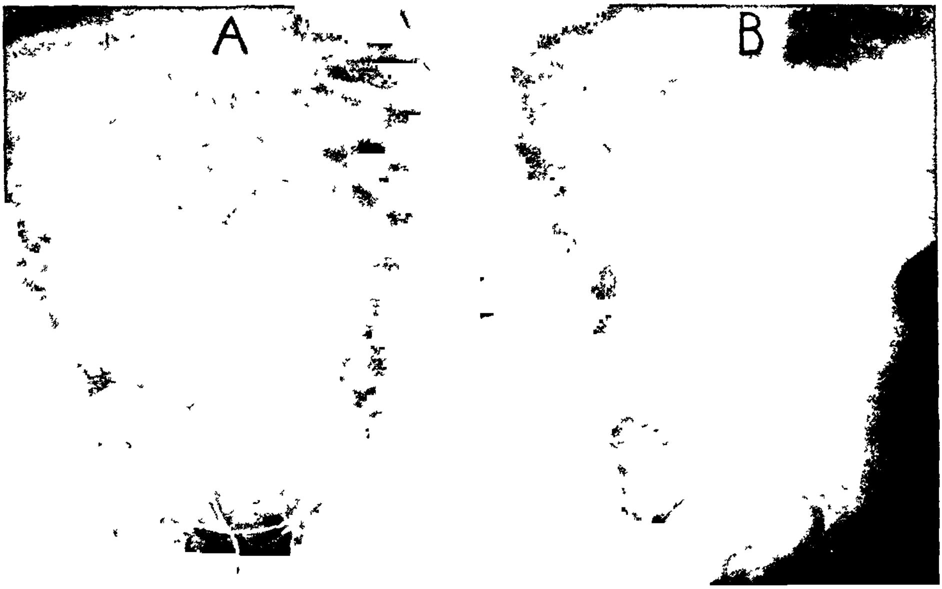


Fig. 3. Case 2. *A*, Ureteropyelogram with catheter inserted in right ureteral orifice situated on lateral surface of cyst which is indicated by filling defect in cystogram. *B*, Dilated lower ureter visualized after puncture of cyst and injection of skiodan.

Cystoscopy on November 29 demonstrated cloudy bladder contents in the presence of a normal vesical mucous membrane. The left and a right ureteral orifice were identified and catheterized. A cystic mass was situated on the right side. A tortuous right dilated ureter and dilated pelvis were visualized (fig. 3, *A*). The pelvic pattern suggested this was the caudal pelvis of a double kidney. There was a filling defect in the cystogram which was due to the cystic mass arising in the proximity of the right ureteral orifice. This was punctured
with the needle-tipped ureteral cath turbid fluid was aspirated. This
fluid was replaced with an equal am A ureterogram
obtained in this manner demonstra (fig. 3, *B*) and
indicated the previously outlined to the cystic
ending of this ureter. Excretory u subsequently
proved a norma y.

After control phase y was
done on Janua Majo to the

existence of complete pelvic and ureteral reduplication. Both pelves were saccular, the cortex of each pole being replaced with fibrous tissue. A rather marked amount of pyelonephritis was demonstrable microscopically. While not definitely established, because of the pattern and position of the pyelogram (fig. 3, *A*) it is presumed that the cephalic pelvis gave rise to the ureter with a cystic ending because the cystic mass was posteromedial to the patent right ureteral orifice.

Postoperative convalescence was uneventful, the child being discharged on February 14.

At her latest follow-up visit in November 1947 she was noted to be in excellent condition, her urine being crystal clear.

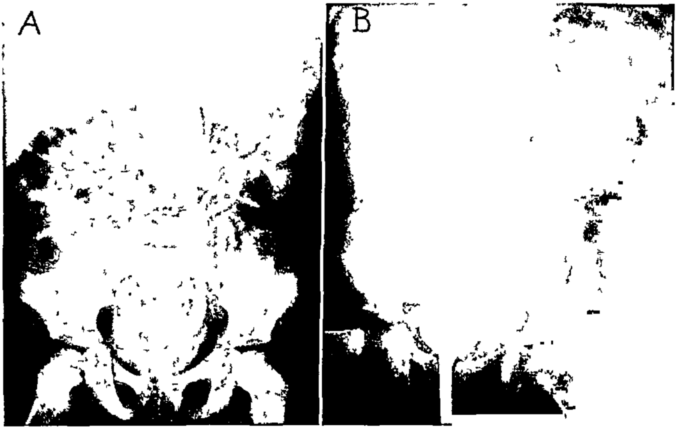


FIG 4. Case 3. *A*, Intravenous urogram visualizing filling defect in cystogram *B*, Visualization of ureter after injection of cystic protrusion

Case 3. S. K. (XR 93560) aged 2 years, a white girl, was admitted to the Riley Hospital on October 30, 1945. The child had been ill for 2 weeks, had a temperature of 102 F., cried with each act of micturition and had mild diarrhea. Findings on admission physical examination were confined to the abdomen, where a painful, ballottable, mobile mass was found in the right flank extending medially to the midline and inferiorly to the crest of the ilium.

Admission blood count showed 10 gm. of hemoglobin and 4,200 leucocytes with normal differential distribution. Urinalysis disclosed reaction acid, trace of albumin and microscopically loaded with pus cells. Blood Mazzini was negative. Initial blood nonprotein nitrogen was 21 mg. per cent. Urea clearance was found to be 17 per cent of normal. Temperature on admission was 100 F.

On October 31 cystoscopic examination of the bladder revealed a large cystic mass occupying the right half of the bladder floor. Intravenous urography demonstrated a normal left kidney pelvis, while the cystogram showed a filling defect on the right side (fig. 4, *A*). With a needle-pointed ureteral catheter the cystic mass was punctured and purulent material aspirated. Skiodan was injected into the cystic mass establishing its identity as a cystic ureterovesical protrusion (fig. 4, *B*). The left ureteral orifice was not identified.

During the preoperative phase the temperature remained elevated for a prolonged period.

On November 23 the patient was subjected to right loin exploration, disclosing a pyonephrotic sac and a thickened, dilated, single ureter. Nephro-ureterectomy was done.

Pathologic examination of the specimen showed a kidney measuring 3 by 3 by 8 cm. in dimension, having a single pelvis. A thickened renal capsule stripped with ease. Inflammatory fibrotic tissue had largely replaced the renal parenchyma.

The postoperative course was uneventful, the temperature reaching normal range on the third day under the influence of penicillin therapy. Discharge took place on the tenth postoperative day. Mild pyuria persisted on discharge.

Follow-up studies have shown intermittent phases of pyuria with cystitis. Further studies to determine the cause for these episodes are contemplated. Generally the child has gained and developed in a normal, healthy manner.

Case 4. G. K. (XR 96120), a 16 month white girl, was first seen at the Riley Hospital on February 1, 1946 with a history of intermittent bouts of fever and the simultaneous finding of pyuria by the family doctor for 10 months.

The child did not appear acutely ill. Her general physical examination was essentially that of a normal child. Urinalysis showed a cloudy appearance, acid reaction, specific gravity 1.010, trace of albumin, and loaded with pus cells. Blood count was normal. The maternal Mazzini was 4 plus; however the child's Mazzini was negative. The blood nonprotein nitrogen was 39 mg per cent.

On February 8 at cystoscopy the bladder was visualized and found to contain a massive noncontractile cystic body protruding from the left lateral bladder wall. No orifice could be found on the cystic mass. The right ureteral orifice was readily identified, catheterized and both urine and pyelogram on that side found to be normal. Attempts to aspirate the cystic mass with a needle-tipped catheter failed. The needle could not be made to penetrate the cyst wall. A lobulated filling defect in the bladder was disclosed by cystogram (fig. 5).

A left loin exploration on February 22 revealed a kidney measuring 5 by 3 by 3 cm. which was removed with generous portions of reduplicated ureters, leading to a double renal pelvic system.

The pathologic report described the cephalic renal pelvis to be supplied by an apparently normal patent ureter. The pelvis was greately dilated, its cortex measuring 3 mm. in thickness. The caudal ureteropelvic system was widely dilated and thinned. The thinned caudal renal parenchyma exhibited abortive glomerular tufts, imperfect tubule formation and wide cystic spaces microscopically.

Postoperatively the temperature reached 104 F. on the first day, gradually falling to normal by the fifth day. The child was discharged on March 18, on her twenty-fifth postoperative day.

Subsequent visits to the clinic have revealed an apparently healthy child, whose urine periodically indicates infection in spite of the usual measures of medical management.

On September 19, 1947 the child was readmitted to the hospital with an acute pyelonephritis episode, her temperature being 106 F. The urine was loaded with pus. After 5 days of intramuscular penicillin therapy the temperature reached normal and the urine was negative. Pyelographic studies revealed very mild ureterectasia in right lowest third.

When last seen on January 17, 1948 the child was well, the urine being negative.

Case 5. L. L. (XL 113678), a 38 year old coal miner, was admitted to the hospital on October 8, 1947 complaining of fatigue, shortness of breath, ankle swelling and dull occipital headaches. The patient began to note nocturia 2 to 3 times during the preceding year, and had experienced episodes of dysuria accompanied by dark foul urine.

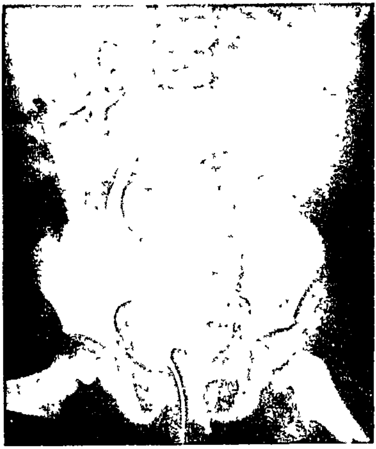


FIG. 5. Case 4. Filling defect in cystogram due to intravesical cystic protrusion. Cyst wall could not be penetrated by needle.

On general physical examination the blood pressure was found to be 255/175 in both arms, supine and erect. The cardiac rhythm was regular, the left cardiac border being 17 cm. left of the midline. An overactive precordium was noted; no murmurs were detected. No evidence of cardiac decompensation was found. An electrocardiogram indicated left axis deviation.

Laboratory findings on admission showed a normal blood count; the urine reaction was acid, specific gravity 1.019, quantitative albumin 0.216 gm., 2–5 hyaline casts and an occasional pus cell. The blood nonprotein nitrogen was 33 mg. per cent. Urea clearance was 36 per cent of normal. An excretory pyelogram indicated a nonfunctioning left kidney, with a somewhat larger than normal right kidney, possessing a normal pelvic pattern.

Cystoscopy on October 21 disclosed a normal lower urinary tract with the mass was punctured and purulent material aspirated. Skiodan was injected into the cystic mass establishing its identity as a cystic ureterovesical protrusion (fig. 4, *B*). The left ureteral orifice was not identified.

During the preoperative phase the temperature remained elevated for a prolonged period.

On November 23 the patient was subjected to right loin exploration, disclosing a pyonephrotic sac and a thickened, dilated, single ureter. Nephro-ureterectomy was done.

Pathologic examination of the specimen showed a kidney measuring 3 by 3 by 8 cm. in dimension, having a single pelvis. A thickened renal capsule stripped with ease. Inflammatory fibrotic tissue had largely replaced the renal parenchyma.

The postoperative course was uneventful, the temperature reaching normal range on the third day under the influence of penicillin therapy. Discharge took place on the tenth postoperative day. Mild pyuria persisted on discharge.

Follow-up studies have shown intermittent phases of pyuria with cystitis. Further studies to determine the cause for these episodes are contemplated. Generally the child has gained and developed in a normal, healthy manner.

Case 4. G. K. (XR 96120), a 16 month white girl, was first seen at the Riley Hospital on February 1, 1946 with a history of intermittent bouts of fever and the simultaneous finding of pyuria by the family doctor for 10 months.

The child did not appear acutely ill. Her general physical examination was essentially that of a normal child. Urinalysis showed a cloudy appearance, acid reaction, specific gravity 1.010, trace of albumin, and loaded with pus cells. Blood count was normal. The maternal Mazzini was 4 plus; however the child's Mazzini was negative. The blood nonprotein nitrogen was 39 mg per cent.

On February 8 at cystoscopy the bladder was visualized and found to contain a massive noncontractile cystic body protruding from the left lateral bladder wall. No orifice could be found on the cystic mass. The right ureteral orifice was readily identified, catheterized and both urine and pyelogram on that side found to be normal. Attempts to aspirate the cystic mass with a needle-tipped catheter failed. The needle could not be made to penetrate the cyst wall. A lobulated filling defect in the bladder was disclosed by cystogram (fig. 5).

A left loin exploration on February 22 revealed a kidney measuring 5 by 3 by 3 cm. which was removed with generous portions of reduplicated ureters, leading to a double renal pelvic system.

The pathologic report described the cephalic renal pelvis to be supplied by an apparently normal patent ureter. The pelvis was greately dilated, its cortex measuring 3 mm. in thickness. The caudal ureteropelvic system was widely dilated and thinned. The thinned caudal renal parenchyma exhibited abortive glomerular tufts, imperfect tubule formation and wide cystic spaces microscopically.

Postoperatively the temperature reached 104 F. on the first day, gradually falling to normal by the fifth day. The child was discharged on March 18, on her twenty-fifth postoperative day.

Subsequent visits to the clinic have revealed an apparently healthy child, though less severe, had occurred and spontaneously subsided over a period of 2 years.

The temperature was 101.6 F. There was rigidity in the McBurney area, psoas muscle spasm and tenderness in the right pelvic region by rectal examination. Urinalysis demonstrated 0.104 gm. of albumin per 100 cc, loaded pus cells, 20–30 red cells and acid reaction. The blood count was normal.

The diagnosis of acute appendicitis being made, an exploratory McBurney incision was made disclosing a normal appendix and a greatly enlarged right kidney. Appendectomy was performed.

On February 15 cystoscopic examination revealed upon the right side of the trigone a cystic mass upon the superior surface of which was easily identified a ureteral orifice. This was subsequently visualized in the cystogram as a filling defect (fig. 7, *A*). Indigo carmine appeared from the left orifice in 12 minutes and from the right in 13 minutes. Intravenous pyelographic studies disclosed a right pelvic system, presumably a caudal component of a complete reduplication, which was displaced downward and laterally (fig. 7, *B*) but not displaced anteriorly (fig. 7, *C*). Puncture of the cyst with the injection of skiodan was requested but was not done.

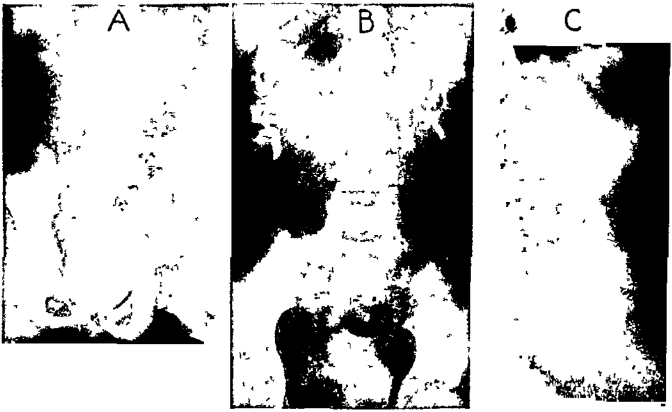


FIG. 7. Case 6. *A*, Filling defect in cystogram due to cystic protrusion into bladder. *B*, Antero-posterior pyelogram of displaced right kidney. *C*, Lateral pyelogram indicating by its pattern caudal pelvis of double kidney had been injected.

On March 1 a right loin incision was made, exposing a kidney possessing pelvic and ureteral reduplication. The caudal pole was essentially normal, however adherence of the two ureters made heminephrectomy technically impractical, so nephrectomy was done.

Pathological examination of the specimen confirmed the clinical findings, the superior pelvis being saccular, its cortex being replaced by fibrous tissue infiltrated by lymphocytes. Its ureter was dilated, thickened and intimately applied to its normal partner which led from a normal caudal pelvis.

Convalescence after the surgical procedure was uneventful. The urine was subsequently clear and the patient was discharged from the hospital on March 22.

Follow-up visits have demonstrated a normally developing, healthy child, her last contact being made in October 1945.

TREATMENT

Treatment was directed toward promoting drainage of the cystic ureter and removal of nonfunctioning, infected renal tissue. It is not uncommon to find these ureterovesical cysts of such size as to seriously interfere with good bladder drainage. These masses may be obliterated by electrocoagulation when necessary. Removal of nonfunctional infected renal tissue was carried out in 5 of our 6 cases; one refused surgery. It is of interest that we were unable to conserve renal tissue by heminephrectomy in any of our reduplications, due either to extensive periureteral fibrosis preventing satisfactory separation of the ureter, or to destruction of the associated renal parenchyma.

SUMMARY

A brief summation of the 38 reported cases of ureterovesical cysts is presented. Abbreviated case reports of 6 instances of this lesion encountered in our experiences are added. In our series 4 of the 6 were children; 5 were females. Ureteropelvic reduplication was found in 21 of 32 instances in the literature, an incidence of 65 per cent, and in 4 of 6 in our experience, for a total incidence of 25 in 38, or virtually 66 per cent.

Identification of the cyst is made at cystoscopy. Cystography frequently will corroborate the presence of the protrusion.

A method of radiographic visualization of the cyst and the associated dilated ureter is mentioned.

Treatment consists of the removal of the infected, nonfunctional renal tissue. Resection of the cyst transurethrally may be performed when indicated.

1711 N. Capitol Ave., Indianapolis, Ind.

REFERENCES

Bostroem: Beitrage zur pathologischen Anatomie der Niere. Freiberg, 1884.
Bottomley, J. F.: Certain congenital strictures of the ureter. Ann. Surg., **52**: 597–625, 1910.
Chwalle, R.: Process of formation of cystic dilatations of vesical end of ureter. Urol. & Cutan. Rev., **31**: 499–504, 1927.
Dourmashkin, R. L.: Blind ureterocele. Urol. & Cutan. Rev., **39**: 783–791, 1935.
Eisendrath, D. N. Congenital strictures and spiral twists of ureters. Ann. Surg., **65**: 552–559, 1917.
Michon, E.: Cystic ending of a ureter. J. d'urol., **36**: 74–77, 1933.
Muschat, M.: Ureterocele of supernumerary ureter. International Clinics, 44th series, **1**: 159–162, 1934.
Regner, H.: Uber die blasenformige Vorwolbung des angebornen Verschlossenen vesikalen Hanleerendes. Inaugural Dissertation zur Erlangung der Doctor-wurde, Giessen, 1910.
Sargent, J. C.: Blind ureterocele. Case report. J. Urol., **35**: 449–503, 1936.
Spooner, C. M. and Lindsay, M. L. Intravesical ureteral cyst. J. Urol., **17**: 453–459, 1927.
Uglew, R. K.: Ein fall von ureterocele eines akzessorischen atresierten harnleiter. Ztschr. f. Urol., **24**: 582–587, 1930.
Young, E. L.: Ureterovesical cyst. J. Urol., **29**: 99–105, 1933.

THE JOURNAL OF UROLOGY
Vol 61 No 3, March 1949
Printed in U S A

TRANSPLANTATION OF THE URETER IN INTRACTABLE VESICAL TUBERCULOSIS[1]

ARTHUR JACOBS

From the Urological Department, Glasgow Royal Infirmary, and the Robroyston Sanatorium, Glasgow Corporation, Scotland

Tuberculous vesical contracture with a progressive diminution in the capacity of the bladder until this is of thimble like dimensions, is a sequel of renal tuberculosis more common I think than is generally appreciated A nephrectomy or nephro-ureterectomy is carried out for a unilateral renal lesion and is not followed by the expected improvement in the symptoms arising from the secondary tuberculous cystitis On the contrary, the frequency gradually increases until in the course of a year or longer the patient is compelled to void with pain every 15 to 20 minutes night and day and finally may become totally incontinent A similar state of affairs can of course arise when the remaining kidney is the seat of, or later develops a tuberculous focus from which tubercle infected urine is discharged into the bladder and from bilateral renal tuberculosis that has been deemed inoperable from the outset

Why a progressive vesical contracture should take place in unilateral disease after removal of the infecting focus is not clear The spread of tuberculosis in the bladder occurs as a rule throughout the submucosa but it is when the musculature is invaded that contracture results In the absence of bacterial infection after nephrectomy there would appear to be some support for the theory that the infiltration of the bladder walls is a response to tuberculous toxins

Whatever the explanation of the cause of this condition, the consequences are well known The ever present demands of the bladder to be emptied reduce the sufferers to a state of chronic invalidism There is another factor, however, that is also of extreme importance As a result of the vesical contracture a gradual destruction of the remaining kidney may occur, even when it is free from tuberculous infection This may be due to the spreading bladder inflammation involving the ureteral orifice and intramural portion of the ureter with consequent stricture or, if the ureteral orifice is incompetent, to back pressure from a bladder in a state of persistent systolic contracture The grave consequences that may ultimately ensue from these factors are well illustrated in the following case history

A woman of 55 years on whom I had carried out a right nephrectomy 12 years previously for unilateral renal tuberculosis was re admitted to the hospital following a transient attack of complete anuria which had lasted 36 hours There had been associated painful swelling in her solitary left kidney which resolved with the spontaneous resumption of the urinary excretion Six months before her re-admission, up to which time the frequency had been stabilized at about 2-hourly intervals, the periods between voiding gradually diminished until ultimately micturition was taking place every 20 minutes night and day. She was now totally incontinent. Examination showed the bladder capacity to be limited to a few cubic centimeters. Excretion urography resulted in a poorly concentrated left pyelographic shadow faintly depicting dilated calyces. The urine was negative for tubercle bacilli. Transplantation of the left ureter was carried out in spite of the thumb-like caliber of the ureter encountered at the operation. Subsequent examination of the urine collected immediately after division of the ureter showed it to be tubercle negative. Now, 6 months later, the patient has a diurnal frequency of 4 every to 5 hours and can sleep all night without disturbance. She leads the normal existence of a housewife and can indulge in a 5 mile walk.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass , May 18, 1948

During the past few years I have been carrying out ureteral transplantation for this condition with increasing frequency. Deviation of the urine away from the bladder by means of nephrostomy or ureterostomy is not a satisfactory procedure for the average patient either from the social or economic point of view. I occasionally employ ureterostomy when the remaining kidney has become affected with an ulcerocavernous lesion and the consequent state of the ureter renders transplantation a real hazard. A lesion in the kidney without infiltration in the walls of the ureter even though the lumen be quite markedly dilated need not however be a deterrent to the operation.

The existence of active extra-urinary tuberculous lesions which render the probable life expectancy a short one might also be an indication for ureterostomy rather than transplantation. Occasionally, in bilateral disease I may remove the kidney most affected and transplant the ureter of the other as in the following example:

A woman of 50 years was admitted to the Urological Department in the Glasgow Royal Infirmary with complete urinary incontinence of 4 years, duration. Illness had commenced 8 years previously with a tuberculous spinal lesion for which she had been immobilized for 3 years. Urinary symptoms started in the second year and an increasing degree of frequency was followed by total incontinence, this taking just over 2 years to develop after the onset of the initial bladder symptoms. The spinal lesion had healed yet she was compelled to lead the life of a recluse for she was constantly wet. Excretion urography showed evidence of gross cavitation in the right kidney with a minor degree of involvement of the left which incidentally had a complete duplication of the ureter. I removed the right kidney and 3 weeks later transplanted the two left ureters. When she left hospital she had perfect control and could retain urine up to 4 hours with longer intervals at night.

OPERATIVE TECHNIQUE

With regard to the mode of operation, I have for the most part adhered to the Coffey No. 1 technique just as I have done with transplantations performed for other conditions. Some minor modifications have been introduced which I consider have added to the safety of the operation. Perhaps the most important of these is the retroperitonealization of the whole site of anastomosis by stitching

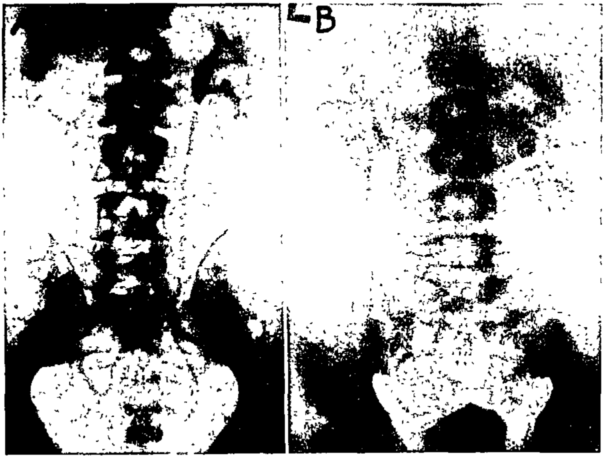


FIG. [illegible] one year after right nephrectomy. Bladder is o[illegible] dilated. Patient suffered from frequency every 3[illegible] can be seen communicating with upper calyx.

B, intravenous urogram of boy aged 16 suffering from frequency every 20 minutes. Vesical contracture depicted, and there is moderate dilatation in lower end of left ureter. Right kidney is seat of massive calcification and consequent autonephrectomy entailed transplantation of left ureter only.

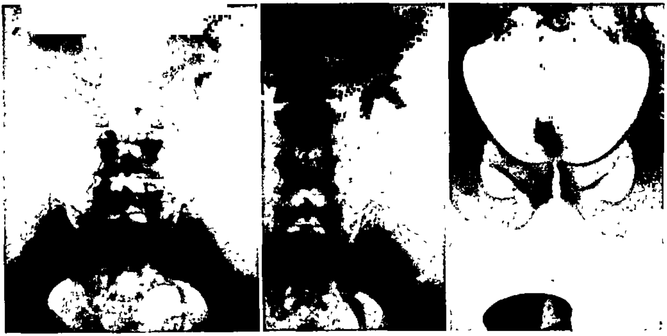


FIG. 2. *A*, intravenous urogram, showing tuberculous cavitation in right kidney and normal left pyelographic shadow. *B*, left kidney 16 months after right nephrectomy had been done. Dilatation which has taken place is result of back pressure from vesical contracture. *C*, showing thimble-like dimensions of bladder which resulted in total incontinence. Complete relief obtained by transplantation of left ureter.

the edge of the lateral flap of the posterior parietal peritoneum to the bowel medial to the suture line. I have also occasionally exposed the ureter through an oblique extraperitoneal incision, above and parallel to the inguinal ligament.

This extraperitoneal exposure is particularly useful in those cases in which the state of the ureter is in doubt and uncertainty is felt as to the feasibility of accomplishing an implantation. In this latter event, a ureterostomy can be proceeded with and the ostium established at a convenient point on the line of the incision. If on the other hand a transplantation is found to be possible, the parietal peritoneum is opened, a segment of the pelvic colon is delivered and the margins of the opening in the peritoneum stitched to the loop of the bowel. The

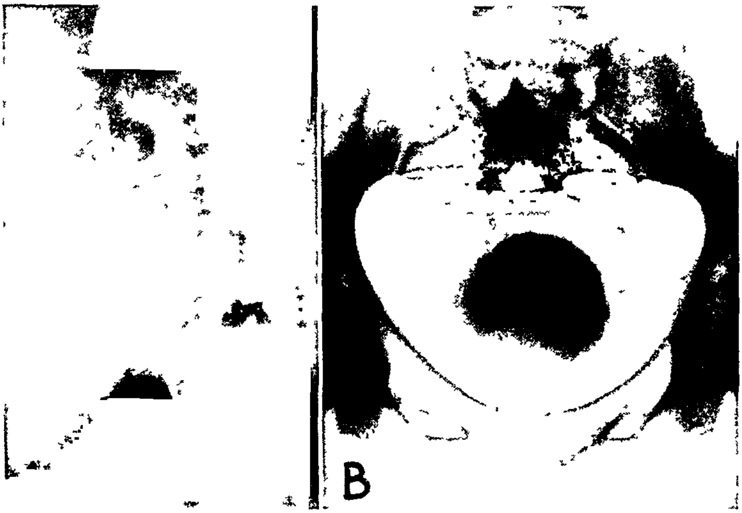


Fig. 3. *A*, intravenous pyelogram taken 4 years after left nephrectomy for tuberculosis. *B*, intravenous cystogram showing moderate vesical contracture. There is evidence of stricture at ureterovesical junction with dilatation in ureter above.

Patient, a man in early thirties, had frequency every 20 minutes. At operation, ureteral lumen was found to be dilated and walls infiltrated. Serosa of pelvic colon was studded with small tubercles but a successful transplantation was accomplished.

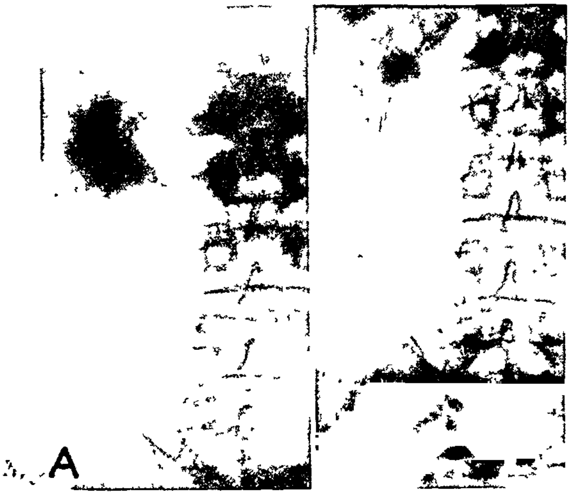


Fig. 4. *A*, marked dilatation in right kidney 5 years after left nephrectomy for renal tuberculosis. Patient had undergone bilateral epididymectomy in intervening period and had developed a tuberculous urethral stricture. *B*, right kidney after transplantation of ureter. Note almost complete resolution in dilatation.

peritoneal cavity is thus closed off and the transplantation proceeded with as an extraperitoneal operation, the bowel bed being made in that part retained outside the peritoneal cavity. This was the actual procedure used on the 2 cases that I have described.

RESULTS

I have carried out transplantation for tuberculous vesical contracture on 25 patients with a mortality of 4 resulting from the operation. Three of these 4 deaths which took place respectively on the third, seventh and twenth post-operative days occurred with patients who had not only an active lesion in the remaining kidney but also gross changes in the walls of the ureter such as I would now consider a contraindication to the operation. The major number of these operations have been performed during the past 4 years though I have 1 patient, a woman in the early forties, whose right ureter I transplanted 6 years ago, her left kidney having been removed 10 years earlier. She is in full employment as a domestic help and is in good health. Three patients have died from activity of their extra-urinary lesions, 2 within 2 months of the transplantation, 1 after the elapse of 2½ years. *One young girl of 18 died suddenly from uremia 8 months* after operation. She had had a right nephrectomy at the age of 6 and had been totally incontinent for a year. She also suffered from an active knee joint lesion.

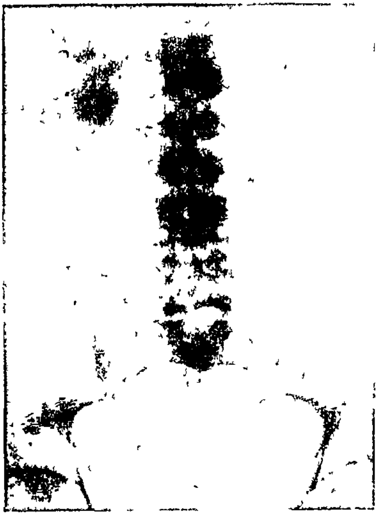


FIG 5 Intravenous urogram, showing gross tuberculous involvement of right kidney with a minor lesion in left, on which side there is complete duplication of ureter. Note contracture of bladder which caused patient to have total incontinence A right nephrectomy was done and 3 weeks later the 2 left ureters were transplanted into pelvic colon.

I successfully transplanted a ureter the dimensions of which approached small bowel though the walls were soft and flaccid. Up to the time of her death she had complete rectal control and could retain urine for 3 to 6 hours. Of the remaining patients, a number are gainfully employed and all are gratified with the relief they have obtained. It may be that streptomycin or some other bacteriostatic to which the tubercle bacillus is vulnerable will prevent this serious aftermath of renal tuberculosis. If so, the need for deviating the urinary stream away from a bladder that can no longer perform its function, will not arise.

The reader is referred to figures 1 to 5.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

DISCUSSION

DR. GEORGE FISH (New York, N. Y.): It is a privilege to meet Mr. Jacobs and a rare opportunity to appraise the fine talents he has devoted to a group of sufferers who are perhaps the most miserable group of people in the world. He deserves thanks and praise.

Mr. Jacobs, in his transplanting of ureters, does not leave entirely clear in my mind some of the indications which led him to use this operation, and I am not sure from his discussion just what efforts were made to determine whether or not the ureters he transplanted were infected with tuberculosis before the transplanting.

It has been our experience in this country, as noted in the work of Colby and others, that stricture formation is a common thing in ureters, whether they are transplanted to the skin or the bowel, and one wonders whether, as time goes on, some of these cases of Mr. Jacobs may not develop strictures. If they do, as he has mentioned in his paper, he is quite ready and willing to use intracutaneous ureterostomy, and I thought before he left he might like to see a rather novel cutaneous ureterostomy we have developed in our clinic recently with the co-operation of Dr. Stevenson of the Department of Plastic Surgery.

(Slide) It consists in the formation of a solid pedicle graft as shown on this slide.

(Slide) The next procedure in the operation is to expose the ureter through a lumbar incision, cut it off near the bladder, pass a scalpel through the pedicle, then tie the distal end of the ureter to the scapel and pull it through the pedicle, stitching the ureter only at the opening in the pedicle.

(Slide) Here you see the ureters coming down through two pedicles. There are no sutures put in the ureter except around the meatus. Primary healing was the result in the 2 cases we have done and the patients are comfortable. The apparatus used to collect the urine is shown here. It will be modified later.

(Slide) And here are the two patients, two-gun Annie and three-barrel Pete. They have both been relieved of intolerable suffering, I hope, for a long time.

DR. MANUEL E. PESQUEIRA (Mexico, D. F.): We, unfortunately, have many cases of urinary tuberculosis in Mexico, and have been performing ureteral dilatation and transplantation of the ureters since long ago. We have seen this dilatation of the ureter on the opposite side of the tuberculous lesion, and I think this is caused by a lesion of the ureter itself and not by the contracture of the bladder. You can see frequently this dilatation with a normal or almost normal-sized bladder.

I want to show you some slides of renal tuberculosis. All of them are excretory urograms taken before operation.

(Slide) We see here the dilatation of the right ureter and a large bladder in a case of tuberculosis of the left kidney.

(Slide) Left renal tuberculosis and right ureter dilatation.

(Slide) The same case. It shows the lower part of the right ureter and the contracted bladder with a double contour.

(Slide) This is a case with an almost normal-sized bladder and dilatation of the ureter.

(Slide) Right tuberculous lesion and dilatation of the left ureter. The bladder is not shown perfectly, but in the next plate you will see—

(Slide) A normal-sized bladder.

DR. OSWALD S. LOWSLEY (New York, N. Y.): I believe that Mr. Jacobs has presented the subject very satisfactorily and completely and agree with most of his points.

It is well to call attention to the fact that it is our duty as physicians not only to heal the sick but also to relieve human suffering, and no one suffers so much as a patient who has intractable tuberculosis of the bladder. It is our custom, when we have a patient suffering from tuberculosis of both kidneys, to remove the bad one, and we have not regretted this practice in a single instance, because the kidney that is not so seriously affected usually carries on and becomes better; in case the bladder is not relieved of the terrific spasms, and so forth, we then unhesitatingly transplant the ureter to the bowel, because for some reason or other the bowel seems to handle tubercle bacilli better than the bladder.

I will simply quote 1 case, the first one that we did, a woman who had terrific symptoms, voiding every 10 or 15 minutes, day and night. Dr. Kirwin and I went into a huddle 16 years ago and transplanted her ureter to the bowel, fortunately extraperitonealizing it, because this ureter was dilated to about 4 times the usual size, but her agony was such we thought we had better do it anyway. The patient got a fecal fistula which closed in due course. I have seen this woman within the last month, 16 years after transplantation, and she has lived a happy, comfortable life, and is grateful for the operation which was done at that time.

MR. ARTHUR JACOBS (Glasgow, Scotland): May I thank Dr. Fish, Dr. Pesqueira, and Dr. Lowsley for their remarks. Dr. Fish has mentioned that he wasn't quite sure of my indications for transplantation as distinct from ureterostomy. I will transplant a ureter even from a tuberculous kidney if the walls of that ureter are not infiltrated or indurated. Dilatation of the ureter is not a contraindication.

I do think that no matter how technically excellent a ureterostomy may be, it cannot give the patient the same satisfaction as a successful transplantation.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

RHABDOMYOSARCOMA OF THE URINARY BLADDER[1]

HERMAN J. MEISEL, WILLIAM H. HEATH AND JOSEPH M. MILLER

From the Veterans Administration Hospital, Fort Howard, Md.

Rhabdomyosarcoma of the lower urinary tract is a rare tumor, for a review of the literature disclosed only 32 reported cases. Of these 21, are described as prostatic in origin and the location of 2 was unknown because of the unavailability of foreign publications. Only 9 cases have been reported as definitely originating from and limited to the urinary bladder. It is with this latter group that this report is concerned and to which it adds a tenth case.

Rhabdomyosarcoma of the prostate, it is generally agreed, arises from the normal striated muscle which has been demonstrated in the anterior part of the prostate, in the region of the internal vesical sphincter and the adjacent area of the trigone. The source of such tumors within the urinary bladder, however, is not quite so clear, and is hypothetical at best, since striated muscle has not been demonstrated there. It has been suggested that developmental anomalies at the lower end of a wolffian duct may provide such a source. Again it has been postulated that "vagrant sarcoblasts" migrate to the subepithelial layers of the bladder and act as a seed for the tumor. It would seem quite possible that in certain individuals extensions of the normal striated muscle in the lower trigonal area may occur upward into the floor of the bladder, where these tumors are usually located.

Grossly, the rhabdomyosarcoma of the bladder is described as a smooth, nonulcerating, shiny, completely epithelialized tumor attached to the bladder wall by one or more pedicles. It may resemble multiple polyps or approximate an hydatidiform mole in appearance. When the tumor is rapidly growing or very large, as in the present instance, the surface layers receive insufficient blood supply and marked necrosis and sloughing may take place. On microscopic section, the tumor is characterized by spindle-shaped cells, considerably larger than those seen in other types of sarcoma. The cells are multinucleated, ribbon-like, eosinophilic and arranged in broad anastomosing bundles. With the phosphotungstic acid stain, longitudinal myofibrillae can be demonstrated. Marked pleomorphism may be seen and cross striations may be present although these occur only in the highly differentiated tumors. Tumors with large bizarre multinucleated cells with ribbon-like cystoplasm are apt to be rhabdomyosarcoma even in the absence of cross striations.

Rhabdomyosarcoma of the lower urinary tract has been reported in individuals aged 1 day to 69 years. Seventy-five per cent have occurred in individuals under 40 and 50 per cent of such tumors in the bladder have occurred under the age of 2 years. There is no significant variation in incidence between the sexes. All the reported bladder tumors have been rapidly growing and quickly fatal, the

---

[1] [illegible] Chief, Medical Director, Department of Medicine and [illegible] ho assumes no responsibility for the opinions expressed

longest survival period after diagnosis being 13 months and the average survival being 6.5 months. Only 1 case showed remote metastasis, the typical mode of growth being by direct extension and invasion. The initial symptoms have usually been those of obstruction and ensuing infection. Rarely has there been gross hematuria and more rarely has this been the presenting symptom. Therapy, as one can see from the survival rate, has been uniformly unsatisfactory. It would seem that once the diagnosis is made by the cystoscopic biopsy, as radical a resection as possible should be done. One should immediately resort to segmental resection or total cystectomy, if indicated. Other common methods of treatment of bladder tumor would seem to have no place here. Indeed x-ray therapy apparently has a distinctly stimulating effect on these tumors.

CASE REPORT

A 32 year old Negro was admitted to the Veterans Administration, Fort Howard, Md. with the complaint of gross hematuria with clots for 1 week. The hematuria was severe, continuous, and associated with frequency, dysuria, and episodes of retention due to the clots. There was gradual development of low back pain and generalized weakness. A history of previous genito-urinary complaints was not obtained. Venereal diseases were denied. The family history, the past history and review of systems were noncontributory.

The physical examination was not remarkable except for generalized weakness and marked pallor of the mucous membranes. On rectal examination an indefinite fullness was felt in the region of the posterior bladder wall.

Examination of the peripheral blood revealed the hemoglobin to be 32 per cent, erythrocytes to be 1,280,000 per cubic millimeter, and the leukocytes to be 9,150 per cubic millimeter with a normal differential count. The nonprotein nitrogen was 37.5 mg. per cent, and the Kahn reaction was negative. Bleeding and coagulation times were within normal limits. The urine was grossly bloody and on microscopic examination revealed numerous erythrocytes. Culture of the urine revealed it to be sterile. The roentgenogram of the chest was within normal limits. An excretory urogram revealed an entirely normal upper urinary tract but showed a large filling defect in the lower part of the left wall of the bladder. Cystoscopic examination at this time was unsatisfactory due to profuse bleeding but a mass was dimly visualized.

Initial therapy consisted of copious transfusions of citrated whole blood, bed rest and intramuscular injections of vitamin K. An indwelling Foley catheter was inserted into the bladder and this was irrigated frequently with a 1/4000 solution of silver nitrate. Occasional installations of topical thrombin solution were given. On the sixth hospital day cystoscopy was again performed. This revealed a globular tumor mass about 5 cm. in diameter attached to the left posterior wall of the bladder by a somewhat smaller, but still broad, pedicle. The tumor was markedly necrotic with grayish, sloughing material over most of its surface. The trigone and the ureter orifices were uninvolved and widely separated from the tumor. A cystogram showed the extent of the mass. A biopsy was interpreted and reported as a malignant muscle tumor.

After further citrated whole blood transfusions and other preoperative supportive therapy, surgical exploration was performed by one of us (H. J. M.) on the seventeenth hospital day under spinal anesthesia supplemented by sodium pentothal. Through a low midline incision the bladder was exposed and isolated well below the limits of the tumor, which could be palpated through its wall. The bladder was then opened, exposing a large, globular, necrotic tumor attached to the highest part of the left lateral wall by a solid pedicle about two centimeters in diameter. The remainder of the bladder was normal and the entire tumor was removed by excising, with the electrosurgical knife, the full thickness of bladder wall along a circular line averaging 2.5 cm. from the base of the pedicle of the tumor. The entire operative area was then bathed for about 5 minutes in 70 per cent alcohol. The bladder was then closed in layers around a number 32 F. Foley suprapubic tube and the wound closed with sufficient perivesical drainage. His postoperative course was uneventful save for the formation of a small vesical calculus which was removed cystoscopically 7 weeks after operation. At that time a well healed scar was seen at the site of resection and the capacity of the bladder was found to be 150 cc.

The tumor was the shape of a mushroom 6 cm. in diameter and was attached to the bladder wall by a pedicle 2 cm. in diameter. The weight of the neoplasm was 38 gm. and it was soft, grayish-pink and extremely necrotic. On cut section, it seemed well circumscribed where it was attached to the bladder wall. The cut surface showed irregular yellowish translucent and opaque areas, in some places appearing almost myxomatous.

Microscopic composition[2] of the tumor consisted for the most part of spindle-shaped cells considerably larger than those observed in leioyomas. With hematoxylin and eosin, using the low power objective, the cells were seen to be definitely eosinophilic and arranged in broad anastomosing bundles. Polarity was fairly granular with occasional longitudinal striations. Many of the cells were ribbon-like with central nuclei and broad trailing masses of cytoplasm. Several "tadpole" forms were noted. The occasional presence of giant cells strengthened the resemblance to typical rhabdomyosarcoma. Mitotic figures were present but none was pathologic. Cross striations although carefully sought for were not encountered.

The last follow-up examination was done 6 months after operation. The patient did not have any urinary complaints, had gained 15 pounds in weight and was again working as a railroad switchman. At this time the urine was microscopically clear and sterile on culture. There was no evidence of recurrence intravesically by cystoscopy or extravesically by bimanual examination.

SUMMARY

Pertinent findings from a review of the nine reported cases of rhabdomyosarcoma of the urinary bladder have been discussed.

A tenth case of such a tumor has been reported.

---

[2] The microscopic pathology has been graciously reviewed and confirmed by Dr. M. B. Dockerty of the Mayo Clinic, Rochester, Minn.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

PHYSIOLOGICAL PRINCIPLES GOVERNING THERAPY OF THE NEUROGENIC BLADDER

J. SYDNEY RITTER AND ANDREW SPORER

From the Urology Service of the Goldwater Memorial Hospital, New York, N. Y.

The care of patients with lesions involving the nerves of the bladder has always been a difficult and complicated problem. This was attributable not alone to the complicated analytic and pathological aspects, but also to the fact that no definite therapeutic principles with a rational approach had been established. Without the latter, a treatment could only be empiric, only too often purely symptomatic. The lack of knowledge concerning bladder physiology has been responsible for this attitude. Indeed many aspects of the neurophysics of the bladder function in some respects are still incompletely understood.

Considerable progress has been made within recent years in our treatment of the neurogenic bladder. Much of this has been the result of the observations and studies of Donald Munro, who was among the first to base his system of treatment upon an understanding of the physiological principles of micturition. The improvements in results with his technique have given an impetus to further study of the physiological mechanisms of bladder control, with the hope of obtaining additional therapeutic aids.

A knowledge of the normal mechanism of micturition is essential to understand the variations accompanying the pathological changes. Formation of urine is continuous; yet we do not urinate continuously. This is due to fact that the sphincter at the bladder exit does not open, and the detrusor muscle of the bladder is not in a state of constant systole. It is essential that a stretch reflex first occur before these two necessary functions of micturition come into play. The stretch reflex is the basis, therefore, of normal micturition. Its mechanism is as follows:

The continuous flow of urine into the bladder distends the bladder musculature. However, rather than the stretch reflex being called into play, the bladder musculature adjusts itself to the increased pressure by relaxing and, thereby, increasing the capacity of the bladder. This process continues pari passu with the formation of urine, but it is not unlimited. When the limit of normal elasticity of the detrusor fibers is reached, then the connective fibers present between the muscle fibers are also stretched. This brings the stretch reflex into play, because the nerve endings situated in this area are thereby stimulated. The afferent fibers of the nerve endings in the connective tissue travel through the posterior roots of the II, III, IV sacral nerves to the corresponding levels of the spinal cord. These fibers are connected to the anterior root cells, whence the efferent fibers to the detrusor originate.

The above description of the stretch reflex is oversimplified for clarity. Actually afferent impulses reach the spinal centers all during the process of distension of the bladder. However, the summation of these stimuli is not sufficient to bring forth the stretch reflex. When the bladder distention is sufficient to produce a stretch reflex, this may be inhibited by interference with the reflex by higher (cortical) centers. Conversely the reflex may be evoked by the same influences before complete bladder distention would normally produce it. This is established, as we may observe in ourselves, by relaxation of the perineum, increase in intra-abdominal pressure, and contraction of the abdominal wall; thereby producing increased bladder tension and consequent stimulation of the nerve endings within the bladder wall, initiating the stretch reflex. It should, however, be clearly understood that this voluntary process does not include relaxation of the external sphincter. It merely produces a set of circumstances, which initiate the stretch reflex. The stretch reflex in turn is responsible for the opening of the sphincter. Opening of the sphincter is not under voluntary control. The importance of this phenomenon will be discussed later.

Several observers have suggested other afferent parts of the reflex arc than that described above. Goltz, for example, in 1874 believed that the sensory portion of the reflex arc was derived from the posterior urethra. He postulated that increased intravesical pressure caused the passage of urine into the posterior urethra, where its presence initiated the stretch reflex. This has since been shown to be without foundation.

Barrington thoroughly studied this question and described at least six sources of afferent stimulation for the stretch reflex, including pathways originating from the bladder, the anterior, and posterior urethras.

Under normal conditions, all these various points of afferent stimulation are simultaneously excited.

The mechanism of the external sphincter is less clearly understood. The initiation of the stretch reflex results in its opening to allow the passage of urine, but it is not known whether this is due merely to increased pressure, based upon the contracture of the detrusor overcoming the constant tone of the external sphincter, or whether active dilatation of the sphincter, similar to the Sherrington reflex, accompanies the contraction of the bladder. In any case, the external sphincter closes immediately upon the complete emptying of the bladder. There is evidence that the closure of the internal sphincter is more gradual. Unlike the opening of the external sphincter, secondary to the stretch reflex, the closure of this sphincter can be brought about voluntarily.

Finally, recognizing that the main afferent pathways of the stretch reflex pass through the II, III, IV posterior sacral roots, various sensory pathways from the bladder exist, accompanying the sympathicus. The sensation of a distended bladder may also arise from pressure on the nerve ending in the peritoneum.

More than 50 years ago, the earliest effort to record vesical activity was attempted. The recorded vesical activity contributed in many ways to our knowledge of the physiology of micturition. It was hoped that cystometric studies would aid in the interpretation of the altered vesical activity due to central and peripherical diseases.

The earliest recording of vesical activities were probably done by Mosso and Pellacani in 1882. Their study was very accurate, and the interpretation of the obtained waves due to vesical and extravesical influences has remained essentially the same.

Cystometric studies, recording vesical activities, was popularized after 1918, and its use was introduced in this country around 1927 by Rose. To perform this examination numerous instruments were manufactured. They all work well and satisfactorily. The type of instrument is not important. The value of the study lies in the correct interpretation and evaluation of the recorded waves, and its application to the clinical findings.

Just the recording of the vesical activity is not sufficient to obtain satisfactory information. The subjective changes noted during cystometric studies, during each phase of the examination is extremely important. If we apply the obtained recordings to the clinical findings, it will clarify our understanding as far as the pathogenesis and pathology are concerned.

During these years of study, it was established that about 200 cc of bladder capacity is required to elicit the sensation of urination. At about 400 cc there is a strong desire to void, and at around 500 cc of bladder capacity a stretch reflex is elicited. This stretch reflex will cause the contraction of the detrusor muscle, and urination will follow.

It was also noted that under normal conditions the bladder empties itself entirely as soon as the stretch reflex is begun.

When the activity of the bladder function was recorded, it was noted that the intravesical pressure is very low, usually below 10 cm. of water, and only raises—and then very sharply—when we are about to elicit the stretch reflex. This reflex can produce an intravesical pressure as low as 20 cm. of water and even as high as 150 cm. of water. The height of pressure will depend on the strength of the detrusor. We can raise the intravesical pressure above 100 cm. of water just by contracting our abdominal muscles and pressing the bladder. This pressure will increase and decrease, in proportion, the strength of the abdominal pressure, and it will cease immediately after the pressure of the abdominal muscles is released.

It was noted that the normal bladder capacity in any particular individual is remarkably constant. The recorded waves, which occur when the stretch reflex is produced, are fairly equal in height. It was also noted that normal vesical activity can and does occur without the help of the abdominal muscles. The stretch reflex can be elicited in a curarasized animal or in an anaesthetized human

The center in the sacral cord is under central control, but it can function fairly satisfactorily independently of the higher centers. In newborns, until the higher centers develop, the center in the sacral cord regulates the urination through the stretch reflex. It appears that the function of the higher centers is mostly inhibitive.

If we summarize our knowledge from the physiology of micturition, we know that urination is a centrally controlled stretch reflex. The peripheral center lies in the sacral segment of the spinal cord, and the pathway of the stretch reflex is through the II, III, IV sacral segments. There are higher centers in the hypothalamic area, and there is probably cortical representation of bladder function. These higher centers are mainly inhibitors, preventing an untimely stretch reflex.

Diseases affecting the higher centers, or the peripheral center in the sacral cord, or any part of the reflex arc, which destroy or eliminate the stretch reflex, alter the entire physiology of micturition. The study of this altered physiology was a very complicated one, especially since a few wrong principles were introduced during the study of neurogenic bladders, before the normal physiology of micturition was well understood. After years of study, and after the fundamental work of Frederick G. McLellan, Donald Munro, and others, we obtained a fairly satisfactory understanding of the pathogenesis of the neurogenic bladder. There are numerous diseases and pathological conditions which can disturb and destroy the normal physiology. Several attempts were made to classify these diverse causes. The most accepted classification is that of McLellan, who lists the various types of neurogenic bladders in four categories: 1. Uninhibited neurogenic bladder, failure of development, acquired loss of cerebral inhibition, hemiplegia, etc. 2. Reflex neurogenic bladder. 3. Autonomous neurogenic bladder. 4. Atonic neurogenic bladder. The first group includes all cases in which the cortical or hypothalamic centers are diseased or destroyed. The cause of this destruction can be congenital lack of development of these centers or any disease which destroys the higher centers. These individuals will lose the central inhibitory activity, the inhibitory control of micturition. However, the clinical picture might be very varied, depending on the type of lesion (i.e. incontinence, loss of control, etc.).

When the spinal column is injured above the level of the sacral cord, impulses from the higher centers cannot reach the sacral segment, and the micturition will be controlled and elicited by the simple stretch reflex. The sacral cord will control the urination. This type of bladder can empty itself with practically no, or very little, residuum. However, the autonomocity of the sacral segment can be disturbed and destroyed rather easily. (Reflex bladder.)

The destruction of the sacral cord will destroy the real center of micturition. No stretch reflex can be elicited, as the centers of both the efferent and afferent arc are destroyed. The contraction of the detrusor fibers will be regulated by the autonomous activity of the individual detrusor fibers. We like to compare this condition to auricular fibrillation. The contracting detrusor fibers do not work together, and the individually contracting detrusor fibers cannot exert sufficient pressure to empty the bladder. This type of bladder has a large residual urine. (Autonomous neurogenic bladder.)

It was noted that when the posterior roots are destroyed, and the reflex arc is interrupted in this way, patients will not be aware of the condition of their bladders. The bladder might be overdistended because of the loss of the sensory pathways; however, these patients lose the sensation of fullness. They have no pain, and no desire to urinate. Part of the reflex arc is destroyed; therefore, the stretch reflex cannot be elicited. (Atonic type.)

If this condition is allowed to go on untreated, the detrusor fibers will be overstretched until their elasticity is lost. The detrusor fibers will be incompetent, and the primary loss of sensation will be complicated by secondary atony. Complete bladder decompensation will be the result.

This type of pathological change can be found, for instance, in tabetic patients with bladder involvements. Their detrusor fibers are overstretched, and inelastic. They have a huge amount of residual urine. When the resistance of the distended bladder is greater than the resistance of the sphincter, an overflow type of incontinence will result.

When the reflex arc is suddenly interrupted, or the spinal column suddenly injured, or diseased, there is a period of "shock", during which no urination takes place. Before the peripheral centers can take over the control, there is a period during which there is no bladder activity. There is no detrusor contraction. There are no waves when cystometric recordings are done. This condition cannot be influenced by any medication. The period might last days, weeks, or months, and there is no satisfactory explanation for this state. We are unable to account for the long delay between the initial disease and the time the lower centers take over.

This period of shock, and the previously described pathological conditions, were studied carefully, and the vesical activity recorded by cystometer. In certain types of neurogenic bladders characteristic waves seemed to be present. During the early studies, an undue optimism ruled the profession. Many believed that eventually the pathology and localization could be determined by cystometry. It was realized, however, rather quickly that the optimism was unwarranted. No diagnosis was possible just from these studies. Some investigators abandoned the practice and were almost willing to discard cystometric study. Of course, until the pathogenesis was clearly understood, no rational treatment could be started. Therefore, the results of the various therapeutic measures were unsatisfactory.

For years urinary retention was relieved by indwelling catheters. Local and ascending infection could not be prevented, and the patients usually died due to ascending urosepsis. Suprapubic drainage replaced the indwelling catheters, until recently, but the results were equally bad. Suprapubic drainage did not prevent the infection, the stone formation, or the ascending infection.

Munro was probably the first who realized the futility of the above methods. He proved that a large number of patients with neurogenic bladders are able to void without residual urine. The patients can be taught how and when to elicit a stretch reflex, how and when to empty their bladders, and remain dry. He showed the importance of preserving the elasticity of the detrusor fibers. It was proven by him, and many other confirmed this observation, that a fair bladder capacity is necessary to keep these patients dry. If a stretch reflex is elicited too often, and at too short intervals, these patients cannot be kept dry.

In spite of the progress in the understanding of the pathogenesis of the condition, and the improved methods of treatment, the results were still unsatisfactory. Many patients still were unable to void, and many had large amounts of residual urine. It was then thought that the peripheral resistance was too great, thereby overstretching the bladder fibers, which lost part of their elasticity. Thus the elicited stretch reflex would be too weak to overcome the peripheral resistance. Therefore, resection of the obstructing tissue was recommended by Emmett and others. The results were improved but still not satisfactory.

Of course, it has to be realized that a destroyed spinal cord cannot be replaced, and certain defects are permanent. The problem was how to attain the best optimal result to enable these patients to void without residual urine, to prevent them from being continously wet from dripping urine, to prevent ascending infection, and to rehabilitate them.

We decided to study this problem years ago with the idea of establishing certain criteria which might be used as a guide in the treatment of the different types of neurogenic bladders.

We utilized proven facts, tried to apply the physiological principles in our treatment and worked out a system which we consider a logical approach toward solving this difficult problem. We knew the difficulties we had to face were many. The pathogenesis of each phase of the disease and criteria for the treatment of each phase had to be determined. We tried to learn the cause of residual urine and the cause of unsatisfactory detrusor function. We had to determine satisfactory bladder capacity and how to obtain this capacity. The patients who had impaired or lost sensation had to be taught how to notice the distention of their bladders just before the stretch reflex is elicited. They had to be instructed as to how to increase the strength of the stretch reflex by the use of their abdominal muscles or by manual pressure. We had to diminish the peripheral resistance, if this was greater than the stretch reflex. We had to learn when a bladder was well compensated, when we might allow these patients a try at urination. We had to determine the early signs of a pending bladder decompensation. This is a strenuous task, not only for the patients, but also for the physician.

The first part of our study was to learn of any anatomical changes which might occur in the bladder musculature after the nerve centers of the bladder are injured. Is the cause of sudden bladder decompensation a disproportional activity of the longitudinal and detrusor muscle fibers? To study this problem we performed a series of experiments on cats.

We established all types of neurogenic bladders. Operations were performed on anesthetized animals, using intraperitoneal nembutal. A series of 6 cats were used to establish a technique for the experiment. The bladder function in cats is controlled by the I, II, III. sacral segment. Not all three segments play equally important parts in controlling the bladder function, but a stretch reflex can be elicited through these three segments.

For further study, we used 12 cats. In 3 we cut the posterior roots of the SI-SII-SIII segment. This operation was done by removing a sufficient amount of laminae to identify the corresponding sacral roots. This is a rather trying operation, for there are not many identifying landmarks. The fibers which go to the femoral and sciatic nerves were identified and followed; these served later as our landmark. Sterile operative technique was employed, using silk as our suture material.

In 3 cats we destroyed the sacral cord. After identifying the SI-SII-SIII segments, all the anterior and posterior roots were divided, and the cord was crushed.

In 3 cats we transected the spinal cord directly above the SI segment, and in the last cats we transected the spinal cord at midthoracic level.

All the animals were kept alive for at least 5 weeks; some of them for over 2 months. The postoperative care of these cats was not easy. A specially trained animal man was used, who was taught to watch these animals and was shown how to relieve their urinary retention by emptying the bladder with abdominal pressure. Constipation was a serious complication, and the relief of this condition was difficult. The cause of 3 deaths was probably due to constipation and its complications, rather than to ascending urinary infection.

In all these cases the bladder and the urethra were removed and serial sections taken throughout the area of the vesical neck, the lateral bladder wall, and the fundus. In none of these cases was any anatomical disproportion between the longitudinal and circular bladder fibers present.

Besides proving that there is no demonstrable disproportion of the bladder muscle fibers, we could not draw any further conclusions from cat studies. Cystometric studies done were not reliable, as they were carried out under anesthesia, which, as we know, basically influences the result. As our aim was to establish criteria for treatment, decortication prior to cystometric study, though they show the uninfluenced activity of the center in the sacral cord, would not have been useful. This would indicate the activity of the peripheral centers, but would eliminate the cerebral control, without which, as we will later demonstrate, the results are unsatisfactory.

If the peripheral resistance is not a disproportional activity of the bladder musculature, we have to localize the point of resistance, using the following rather simple methods: We put a soft rubber catheter in the urethral meatus and connect the catheter to a bulb syringe. The syringe is filled with contrast material, we use diodrast, and we allow the contrast material to run into the urethra by the gravity method. If we check the flow of dye by x-ray, we will see that it will stop at the level of the external sphincter, if there is no anatomical disfiguration or mechanical obstruction present in the membranous urethra. The pressure of the fluid is never more than 10–15 cm. of water pressure. This pressure is much less than the intravesical pressure that any patient can exert who is able to use the accessory "bladder muscles."

If we perform cystograms in patients with neurogenic bladders, we find the following variations at the level of the bladder neck: In a number of cases the fluid level at the vesical neck was round, and no contrast material went through the area of the vesical neck. In certain cases, however, the x-ray films showed a funnel-shaped vesical neck. In these cases a part of the posterior urethra was visualized. We usually found higher amounts of residual urine where the vesical neck was round. This study, with this simple method, clearly demonstrated the evident fact that the obstruction, or rather the peripheral resistance, which is responsible for the residual urine, is between the vesical neck and the external sphincter. This resistance might be increased by a relaxed perineum, which, as we know, is a common finding among patients with this condition. The obstructive area is composed of the prostatic urethra and the external sphincter. In cases with residual urine, the peripheral resistance is evidently greater than the stretch reflex; this resistance has to be diminished. It should be sufficiently high to retain urine in the bladder until the stretch reflex is established.

Our aim, therefore, is to establish a strong enough stretch reflex to overcome the peripheral resistance, to diminish the resistance of the prostatic urethra if necessary, and to preserve a fairly well-functioning sphincter, which will prevent continuous urinary dripping. When these factors are established, we must teach these patients how to recognize bladder sensations with the help of the accessory sensory fibers, how to increase the strength of the stretch reflex with their accessory bladder muscles; and, if the bladder is well regulated, our duty is to maintain the compensation.

The first step is to establish a large enough bladder capacity, without overstretching the bladder musculature. We know that the daily urinary output is between 1000 and 1500 cc. Patients with neurogenic bladders are advised to increase their fluid intake so as to excrete at least 1500 to 2000 cc of urine daily. With about a 2000 cc daily urinary output, about 80 cc of urine are accumulated hourly in the bladder. If we want to make these patients comfortable and to rehabilitate them, we have to increase their bladder capacity to at least 400 cc. If the stretch reflex is established with 400 cc, they have to void only every 4 hours. We know that the normal bladder can easily accommodate this amount without the danger of overstretching the detrusor fibers. This task can be accomplished by putting these patients on tidal drainage. We used the Munro technique.

If the bladder capacity is diminished, or if the bladder is contracted at the time we begin the treatment, we can increase the capacity by gradually lifting the horizontal part of the tubing, which will cause the syphoning. By gradually lifting the height of the water outflow, the bladder capacity can be correspondingly increased. The bladder capacity can be measured by measuring the quantity of fluid which will cause the syphoning. This has to be checked repeatedly at regular intervals.

During this period, the patients are instructed to watch their abdominal sensation. As they are not able to register the bladder sensation accurately through the regular sensory pathway, a certain unpleasant fullness in their abdomens will indicate the distended bladder. They have to be taught to notice this feeling at an early time. While on tidal drainage, we have to fill their bladders daily, elicit the sensation of fullness, and note whether this always occurs at the same capacity. We must make them conscious of this sensation. The higher the injury to the spinal cord, the more difficult will it be for these patients to note the sensation of fullness. We know that this secondary sensation is carried through the sympathetics and the nerves which innervate the peritoneum. It is quite evident and logical that the higher the lesion, the more sensation is lost with a decrease in the aid from the accessory sensation. In these cases the prognosis is poor, not only from the urological but from the general clinical viewpoint. The establishment of a fair bladder capacity, and the instruction of the patients to notice bladder fullness are the prerequisites to a successful result. If these two criteria cannot be established, we will fail in our effort, irrespective of the type of the neurogenic bladder.

While establishing the above two conditions, we do repeated cystometric studies. In reflex and neurogenic bladders, after an indefinite period following the spinal shock, during which no contraction waves occur at the cystometric study, the detrusor activity will recur. The contractility and the strength of the detrusor will gradually increase, and the height of the waves which indicate the detrusor activity will increase. The stronger the contractility of the muscle fibers, the longer will the contraction wave last. These contracting waves are much more marked and much stronger in the reflex bladder than in the autonomous neurogenic bladder. However, we will notice a gradual improvement in the height of the contracting waves even in the neurogenic bladder, although the contracting waves will never be as regular as in cases of reflex bladders.

In tabetic bladders, especially in advanced cases, we do not see contracting waves. We will note that after a few weeks of treatment, when the stretch reflex is elicited, the contracting waves, as recorded by cystometric studies, will be equal in height. At this time our neurogenic bladder is compensated. We consider a neurogenic bladder compensated when the contracting waves are equal in height and last long enough, and the detrusor contraction is elicited at a constant bladder capacity. These compensated bladders work effectively.

The strength of contraction of the detrusor can be increased by teaching the patients how to increase the intravesical pressure with the assistance of the abdominal muscles. The intravesical pressure, just by the use of the abdominal muscles, can be raised to above 100 cm. water pressure and maintained until the bladder is emptied. The abdominal muscles are actually accessory bladder muscles in neurogenic cases. Their role is very important in atonic neurogenic bladders, especially in tabes, where the stretch reflex is not present, and the emptying depends upon the strength of the abdominal muscles.

When a bladder such as this is obtained, we submit the patient to a trial period at normal urination. In autonomous neurogenic bladders, the contracting waves and the stretch reflex are usually not sufficient to empty the bladder. These and the tabetic patients are the ones who resort to their abdominal muscles. If they can empty bladder satisfactorily without residual urine, our only task is to maintain the status quo. They have to be checked at regular intervals. The bladder capacity must be noted and kept constant. Cystometric studies will indicate the status of the detrusor. The impaired regularity of the contracting waves, diminished bladder capacity, and increased amount of residual urine are always signs of decompensation.

If decompensation occurs, the previously described therapy must again be employed until compensation has been reestablished. A patient with cardiac decompensation must remain under medical supervision as long as he lives. This pertains to the neurogenic bladder as well. Despite high contracting waves, with regularity of contractions and good abdominal muscles, together with what appears to be a well-compensated bladder as determined by clinical examinations, some patients will still be unable to void, and they retain a definite residual urine.

In these cases the peripheral resistance is too great an obstruction for even the compensated bladder to overcome. This peripheral resistance is due to obstructive tissue in the prostatic urethra and can be relieved only be removing this obstruction. Careful endoscopic resection can reduce the resistance, so that no residual urine will remain. We prefer repeated resections, so as not to remove too much tissue. It is always possible to remove more tissue at a subsequent sitting than to risk a resultant total incontinence.

In the reflex bladder, when the reflex arc is intact, contractions are usually strong enought to empty the bladder. It is essential, however, that the stretch reflex be kept at an adequate strength. In these cases, resection will seldom be necessary. In the autonomous bladder, where the contractions are neither strong enough nor maintained, although the abdominal muscles may compensate to a degree, there will still remain some residual urine. In these cases resection is indicated.

For the tabetic individual whose detrusor contraction is nil, and whose abdominal muscles play an important role in emptying his bladder, extensive resections are necessary. These patients must be carefully instructed and taught to note the sensation of bladder fullness, so as not to permit overdistention of the bladder and thereby the loss of elasticity of their detrusors. When the detrusor contraction is weak, and the abdominal muscle power lost, progress is very poor. Should the sensation of bladder fullness be lost, treatment is unsatisfactory. It is fortunate that the tabetic patient usually seeks aid before the disease has reached this stage.

Diseases affecting the higher neurogenic centers present varying symptoms, depending upon the area of the central damage. It is not our intention to discuss this type of disease but to state that the prerequisite for satisfactory results is that the patient be fairly intelligent, cooperative, and comprehensive of the various problems. It is, therefore, evident that if the damage in the central nervous system is marked, and the intelligence impaired, our results cannot be good. Disabling diseases, such as deforming arthritis, etc., complicating neurogenic bladder conditions, will also make therapy difficult, if not hopeless.

Prior to the institution of our therapy, and at any time during our treatment, several complications might occur, which would lead to poor results. Infection, which was so deadly prior to the era of chemotherapy, can appear at any time. With the proper use and adequate dosage of antibiotics, intercurrent infection can be controlled. It is advisable to make regular urinary cultures in these patients, so as to prescribe the specific to eradicate all infectious organisms before they cause clinical symptoms.

It is evident that, with the knowledge of the pathological problems to be overcome, factors influencing the results must ever be kept in mind. Here we include delayed therapy, infection resulting in cystic fibrosis, and contracture. This results in a limited bladder capacity.

A constant state of excitability, causing an overactive stretch reflex, will result in a diminished bladder capacity. Should this be present, it will complicate treatment. However, before a decompensation of the musculature occurs, there will be a period during which this muscle will hypertrophy to overcome the resistance. Trabeculation and cell formation will be seen during this period. Between this stage and total decompensation, several diverticula may develop. These diverticula have no muscular wall. As our treatment is partially based on re-establishing the elasticity of the muscle fibers, our result at this stage of the disease cannot be very successful. These diverticula, especially if they are of the retention type, can cause repeated and recurrent infections, which will be an added burden.

Trabeculation can occur in a neurogenic bladder, due to the overactivity of the stretch reflex, causing a hypertrophy of the musculature. If untreated, this would result in the same complications as produced by mechanical obstruction.

The understanding of the physiology of the micturition and the pathogenesis of the disease will indicate that a treatment with a suprapubic drainage is not a satisfactory one. The regulation of the bladder with a suprapubic tube is not easy, although occasionally it can be done. However, we almost always sacrifice at least part of the elasticity of the detrusor fibers. This type of treatment should only be used under emergency conditions, in war areas, where no proper therapy can be instituted for a longer period, or in those cases in which we give up all hope of establishing a well-functioning bladder. We have used it rarely and for a limited period.

The result of the therapy described above was analyzed in our first 50 patients who had neurogenic bladders. The types of cases were as follows:

	Cases
Transverse spinal cord lesion above S1 level	18
Cauda equina or sacral cord injury	10
Tabes dorsalis	16
Poliomyelitis with bladder involvement	2
Anterior and posterior nerve root fiber destruction following abdomino-perineal resection	4

	Satisfactory results for prolonged time	*Failures*
Transverse spinal cord lesion	10	8
Cauda equina or sacral cord injury	7	3
Tabes dorsalis	14	2
Poliomyelitis	1	1
Pelvic lesion	2	2

A large number of our patients were referred in an advanced stage of the disease. They had not had adequate treatment, and, in a number of cases, the damage was irreparable. Some of our patients did not have the ability, intelligence, or will power to cooperate. The combination of these factors was the cause of the high number of poor results. In some of our cases, the therapy, as referred to above, had to be repeated in order to obtain satisfactory results.

TYPICAL CASE REPORTS

To better illustrate our technique, we shall present four typical cases:

Case 1. O. D., 26 years of age, in December 1946, fell while skating. He felt a sharp pain in his back and buttocks, but was able to stand up, walk away, and continue his routine work for 3 weeks. During this period he had a constant, unpleasant, dull backache. Three weeks after his skating accident he tried to lift something, bent forward, and suddenly felt a sharp pain in his back. He was hardly able to climb into bed. He stayed in bed and, a few hours later, he noticed that he was unable to move his legs. At the same time he was unable to urinate.

He was hospitalized in California, and further studies, including lipiodol spinal x-rays, were suggestive of a sacral cord tumor. In January 1947, a laminectomy was performed, and two displaced intervertebral discs were found compressing the cauda equina. The discs were removed. Postoperatively he improved slowly, and within 6 weeks the lesion was localized at the SI-SII-SIII and SIV segment.

After the operation he was put on tidal drainage. Cystometric study revealed complete bladder atony. His clinical condition improved; he was able to walk, but unable to pass urine. To alleviate his urinary difficulties, a transurethral resection was performed. After the resection he was able to void and was discharged from the hospital for further home follow up. He had considerable difficulty emptying his bladder two days after his discharge.

He returned to New York, and, immediately upon his arrival, he had a secondary hemorrhage. On admission to our service, he had 1200 cc bloody residual urine. The bleeding was easily stopped with an indwelling catheter. Two days later the urine was clear, and the catheter was removed. He had 500 cc residual urine at that time. Cystometric study showed an atonic bladder and very markedly impaired sensation with no desire to urinate. (See figure 1, chart 1.)

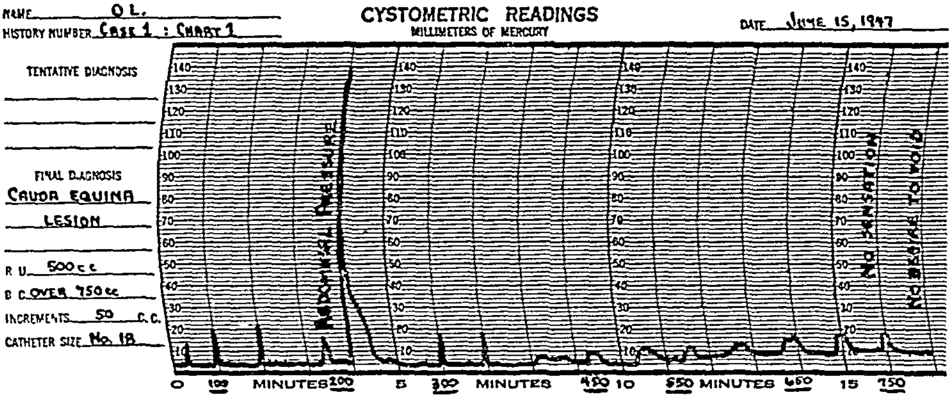
He was placed on tidal drainage, and was taught to observe the sensation of fullness. After 3 weeks on tidal drainage, he was able to observe quite definitely a sensation of fullness and some vague pain at 500 to 650 cc bladder capacity. (See figure 1, chart 2.)

He was able to raise the intravesical pressure with the help of his abdominal muscles over 100 cm. Neurological studies at this time showed saddle anesthesia, cauda equina lesion. Because the neurological improvement was slow, and lipiodol study still showed a block, a second spinal exploration was performed. At this time adhesive arachnoiditis was found, and the adhesions were released. During this time he was on tidal drainage.

After his recovery he still had residual urine. A transurethral resection was done, in July 1947, removing 1.5 gm. tissue, after which he was able to empty his bladder.

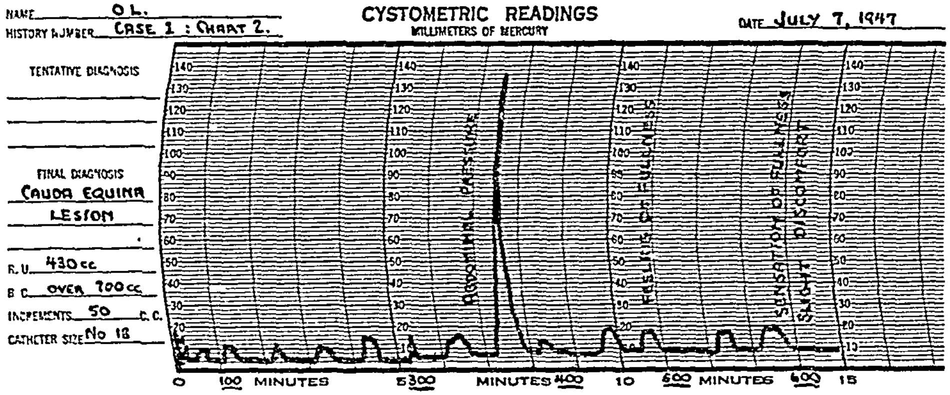
At present he still has a saddle anesthesia. He is able to void without residual urine. A sensation of fullness advises him to empty his bladder, and, with the help of his abdominal muscles, he can do that without residual urine. We see him once a month, just to check the condition of his bladder, to prevent constriction of his vesical neck, and to note any impaired sensation. He is able to do his work.

Case 2. J. H., aged 15, in 1942, at 9 years of age, developed a bad cold. He was running a high temperature. Because his condition did not improve, a physician was called, and he made a diagnosis of pneumonia. The fourth day after the onset of the disease, the child had difficulty moving his legs and was hardly able to pass his urine. His condition rapidly deteriorated, his legs became paralyzed, and he was unable to void.



CYSTOMETRIC READINGS
MILLIMETERS OF MERCURY

NAME O L.
HISTORY NUMBER Case 1 : Chart 1
DATE June 15, 1947
TENTATIVE DIAGNOSIS
FINAL DIAGNOSIS Cauda Equina Lesion
R U. 500 cc
B C. OVER 750 cc
INCREMENTS 50 C.C.
CATHETER SIZE No. 18

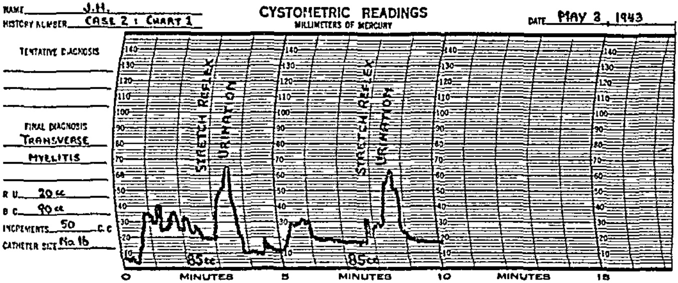


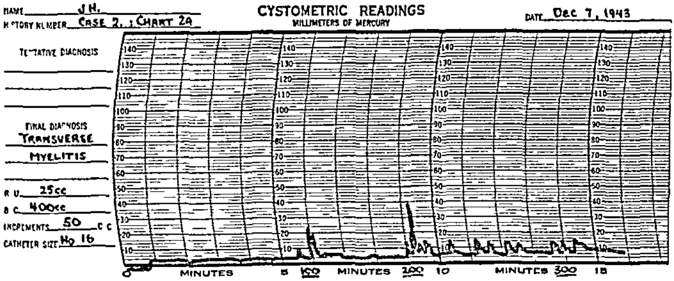
CYSTOMETRIC READINGS
MILLIMETERS OF MERCURY

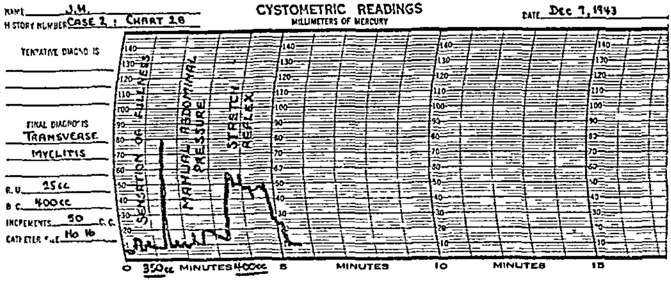
NAME O L.
HISTORY NUMBER CASE 1 : CHART 2.
DATE JULY 7, 1947
TENTATIVE DIAGNOSIS
FINAL DIAGNOSIS CAUDA EQUINA LESION
R. U. 430 cc
B C. OVER 700 cc
INCREMENTS 50 C.C.
CATHETER SIZE No 18

He was admitted to the Neurological Institute, where a diagnosis of transverse myelitis was made. The lesion was at the T7 level. He was treated for 4 months in different hospitals before he was admitted to our service. On admission in May 24, 1943, the child had a transverse lesion at the T7 level. He had cystitis, pyelonephritis, and he was incontinent. Cystometric study showed a reflex bladder with no sensation. The bladder capacity was between 80 and 90 cc. (See figure 2, chart 1.)

He was put on tidal drainage for 4 months. During this time he was instructed to observe a sensation of fullness. The bladder capacity was gradually increased, and, during this 4 month period, we were able to increase the capacity to above 400 cc. Because of the high lesion, it was extremely difficult to teach the child to observe the sensation of fullness with the secondary sensory pathways. Another difficulty was that the abdominal muscle power was almost completely lost, and he could not use these muscles at first to elicit a stretch reflex. This period was often complicated with recurrent cystopyelitis, which was successfully treated each time. After almost six months, he was able to control his urination fairly satisfactorily, with only an occasional premature stretch reflex. At night he was always on tidal drainage. (See figure 2, chart 2, *A* and *B*.)



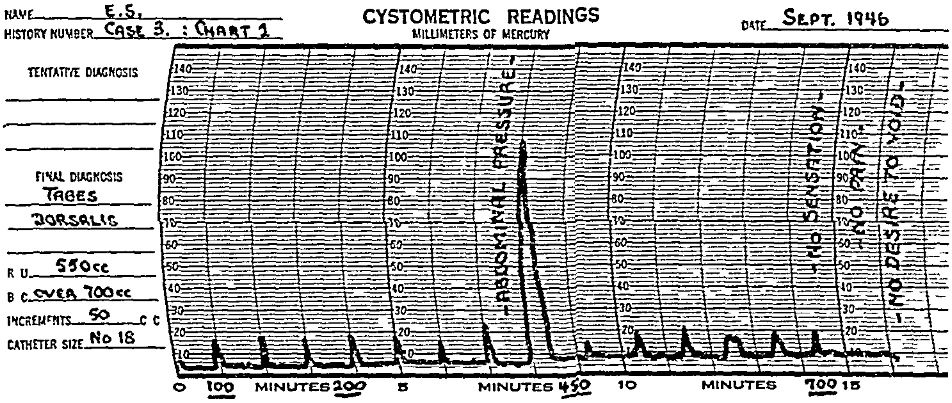




Unfortunately, for over a year we did not see him, and, during this period, a small bladder stone developed (1945). His bladder capacity decreased during this time to 150 cc. In 1946, the above therapy was reinstituted. Fortunately we were able to increase his capacity again. He is able to notice the sensation of fullness. However, he is forced to be on tidal drainage, as the irritation of the stone, if left alone, causes a stretch reflex at irregular intervals. His parents are unwilling to give permission to perform the operation, and, until the stone is removed, the child cannot be brought under control.

This case illustrates the urgency of regular urological surgery.

Case 3. E. S., aged 61, for many years had urinary incontinence. He was able to hold his urine during the day but not at night. He had hesitancy and a weak stream. In 1939, after a hemorrhoid operation, he did not pass urine for 36 hours and had no pain during this time. Examination at that time revealed syphilis, and during the next 4 years he had antiluetic treatment with neosalvarsan and bismuth. During this period he had dribbling, hesitancy, and nocturnal incontinence.



NAME E.S.
HISTORY NUMBER Case 3. : Chart 1

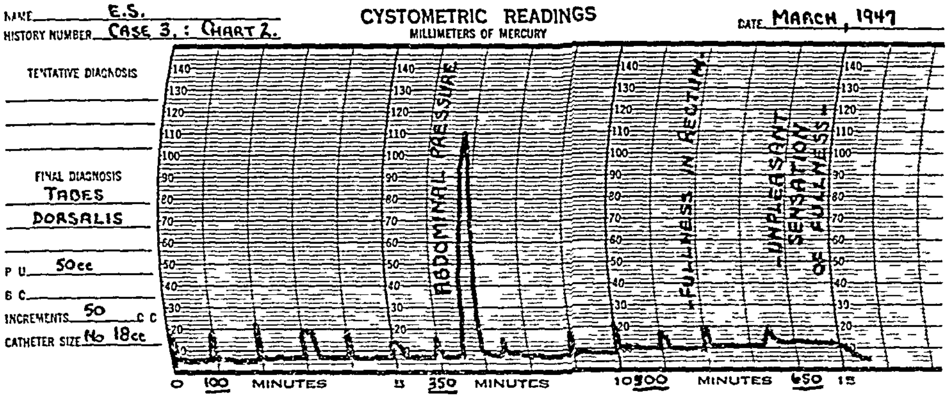
CYSTOMETRIC READINGS
MILLIMETERS OF MERCURY

DATE Sept. 1946

TENTATIVE DIAGNOSIS

FINAL DIAGNOSIS Tabes Dorsalis

R U 550cc
B C over 700cc
INCREMENTS 50 C C
CATHETER SIZE No 18



NAME E.S.
HISTORY NUMBER Case 3. : Chart 2.

CYSTOMETRIC READINGS
MILLIMETERS OF MERCURY

DATE March, 1947

TENTATIVE DIAGNOSIS

FINAL DIAGNOSIS Tabes Dorsalis

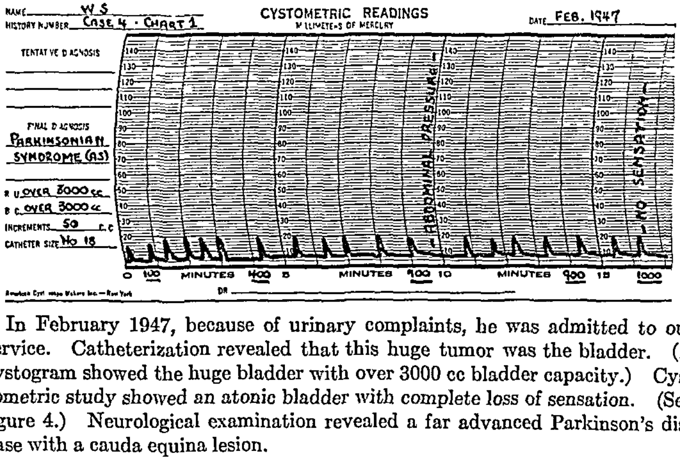
P U 50cc
B C
INCREMENTS 50 C C
CATHETER SIZE No 18cc

In September 1946, he came under our observation. A urological study revealed a small prostate and over 500 cc residual urine. Cystoscopic examination showed a somewhat elevated inferior vesical lip, but no obstructive prostate. He had no bladder sensation, no desire to urinate, and was possessed of an atonic bladder. (See figure 3, chart 1.)

Tabes was diagnosed, and, after neurological consultation, intensive penicillin therapy was started. During this time he was put on tidal drainage and was taught to observe the sensation of fullness of his bladder. A marked pressure sensation in the rectum was first noticed at a 500 cc bladder capacity. This rectal fullness and some unpleasant feeling were elicited between 500 and 700 cc. He was educated to use his abdominal muscles and to increase his intravesical pressure. Because he still had over 250 cc residual urine, in January 1947, a transurethral resection was performed. After the resection, with the additional help of his abdominal muscles, he was able to void without residual urine.

His bladder is still the atonic neurogenic type, but he notices the fullness of his bladder, and, with the help of his abdominal muscles he can void without residual urine. (See figure 3, chart 2.) We see him at intervals to check his bladder and to prevent any deterioration.

Case 4. W. S., aged 59, had had Parkinson's disease for over 15 years. His condition showed gradual deterioration, and, in 1946, he was hardly able to speak. A huge cyst-like tumor was noted in his abdomen in 1941, but no study was done to investigate the nature of this tumor.



In February 1947, because of urinary complaints, he was admitted to our service. Catheterization revealed that this huge tumor was the bladder. (A cystogram showed the huge bladder with over 3000 cc bladder capacity.) Cystometric study showed an atonic bladder with complete loss of sensation. (See figure 4.) Neurological examination revealed a far advanced Parkinson's disease with a cauda equina lesion.

The patient was put on tidal drainage, but we were unable to improve the detrusor tone or to teach the patient to observe any bladder sensation. His abdominal muscles were spastic, and he was unable to increase the intra-abdominal pressure with the use of his muscles. We performed a suprapubic cystotomy after four months of tidal drainage and did three transurethral resections. We did not succeed in establishing any sensation in this bladder, and the patient was unable to void in spite of repeated and very thorough resections.

This case illustrates the hopeless prognosis, if treatment is unduly prolonged, and if the criteria for successful treatment are not present. An interesting feature of this case is that, in spite of the huge distention and full bladder atony, the bladder musculature at histological study, and during the operation, was perfectly normal. No atrophy of the detrusor fibers could be demonstrated.

SUMMARY

The physiology of micturition is discussed.

The pathogenesis of the neurogenic bladder is described and analyzed.

A system of treatment is described, based entirely on physiological principles.

The results are satisfactory if the treatment is started early, if the patients are cooperative, and if there is no disabling central or peripheral disease, which prevents the utilization of the above-described systematic treatment.

A selected group of case histories are presented.

We are indebted to Dr. Julius Rosenthal, Director of Laboratories at the Goldwater Memorial Hospital, for his kind cooperation in carrying out this investigation.

755 Park Ave., New York, N. Y.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

SUDDEN AND COMPLETE DECOMPRESSION VERSUS SLOW EMPTYING OF THE DISTENDED URINARY BLADDER

THEODOR HRYNTSCHAK

From the Department of Urology of the Städtische Poliklinik, Vienna, Austria

Until recently it has been generally believed that the chronically distended urinary bladder should not be emptied abruptly but slowly and gradually for fear of possible fatal consequences. This old theory has been supported by practically all urological schools and textbooks and can be traced back as far as 1844, when Chassaignac openly attributed the death of a patient to sudden decompression of the distended bladder. Literature, especially the French of the bygone century, is full of such publications accusing catheterization and sudden emptying of the bladder of causing such complications as vesical and renal hemorrhages with subsequent oliguria, anuria, and septicemia.

Creevy, however, after a thorough investigation of all the literature prior to 1932, found no serious proof for this old theory. Most probably deaths were due in the majority of cases to an ascending infection of the urinary tract. His study of 71 cases, in which the patients died while under treatment, also shows that there is no conclusive evidence to support this theory. But notwithstanding his scepticism and critical attitude, even Creevy did not entirely free himself of the old belief. He concludes his survey with the following words: "The value of gradual emptying of the chronically distended bladder is therefore open to question, although the complete abandonment of this procedure is perhaps not justified." Hinman also hesitates when he says in his *Principles* and *Practice* of *Urology*: "Infection and not sudden relief of pressure is the problem, and whether decompression minimizes infection remains to be proved."

Thus apart from a few authors who seem to have their doubts about the value and necessity of slow withdrawal of the urine, the old belief is adhered to in all countries even nowadays. As proof of this, a new and improved model of an apparatus constructed for slow and gradual decompression has lately been described by E. L. Brodie.

If such an apparatus is not available, the usual method is that of frequent repeated catheterizations or fixation of an indwelling catheter with partially obstructed lumen, so as to prolong the emptying over as long a period of time as possible. Even the use of an indwelling ureteral catheter in the bladder has been advocated. However, and astonishingly so, gradual decompression seems to have been rarely practiced after suprapubic cystotomy. In these cases it did not seem necessary to follow the old rule.

In 1931 its fallacy was recognized by Brecher and Chwalla, two Viennese urologists. Within 3½ years they treated more than 300 cases of distended bladders by sudden and complete emptying and then inserted an indwelling catheter. I have since then treated all my patients, regardless of the volume of urine, in the same manner. I cannot give the exact number of cases, but the fact that I have kept to this method for the past 16 years seems proof enough that the results have been satisfactory. I have never seen a complication which I could have attributed to sudden emptying, so I have never come back to the old method again. Since then I have treated hundreds of patients. Some have had enormously distended bladders or severe edema of the legs due to compression of the blood vessels by the balloonlike distended bladder. I remember one of my first patients treated by sudden decompression: He was a man of 70 with diabetes, whose bladder yielded over 3000 cc urine. On account of the severely impaired kidney function, he was subsequently submitted to prostatectomy in two stages. No complications whatever occured.

Apart from Brecher and Chwalla I only know of Seifert (1940) who reported 126 cases treated in the same way and with good results. According to him, any attempt at explaining incidental hemorrhages by the ex vacuo theory is fallacious, as it is contrary to all our experiences with hemorrhages in other viscus organs.

Moreover, there are serious drawbacks to the old method of slow decompression. Most of the patients with chronic vesical distension come to us with advanced renal insufficiency and urosepticemia. For such patients immediate action is the course sine qua non for a quick return to normal renal metabolism. The extreme dehydrated condition of the whole organism requires urgent replenishing. Not only the body tissues are in need of water, but also the badly damaged kidney. Kidney function must be restored as quickly as possible by ingestion of large amounts of water to insure the elimination of the nonprotein nitrogen and other metabolites. Since the patient can only start with a large intake of fluid once the bladder has been emptied, slow decompression will cause a delay which may be fatal.

Frequent catheterization or the indwelling catheter will eventually produce urinary infection and subsequent ascending infection. The only therapy against the imminent danger is the immediate onset of a downward flow of urine. Immediate action should be taken to produce abundant urinary secretion. Therefore, sudden decompression enables the patient to start at once with a large fluid intake. We know of no better therapy since even the best sulfa drugs would be without effect because their concentration would be too low during a large fluid intake.

The necessity of enforcing a high fluid intake is now generally recognized, however not the advantages of sudden decompression. Where is the explanation? Have even the great masters of the past been induced into error? For it was their observations and conclusions which led to the theory of slow emptying.

I will try to elucidate some of the errors and add some explanations to Creevy's study.

Sudden decompression of the bladder may indeed bring on those fatal complications feared by our predecessors unless we follow certain rules which will render the proceedings entirely free of danger.

The one outstanding principle is that once the bladder has been emptied by sudden decompression it has to remain empty. Nothing must interfere with the free escape of urine for a single moment for a period of at least 1 week.

All of us know that bladders with a retention of even more than 1000 cc completely lose their elasticity after decompression. Their capacity sinks to almost nothing as has been proven by Rose's manometric experiments. Further evidence of a small bladder capacity is also found in the pains arising from even small quantities of water injected into the bladder, and the fact that the fluid is immediately expelled around the catheter. Therefore, if we do not see to it that the bladder remains completely drained at all times, backpressure towards the kidney may develop at any moment, since the bladder has lost its dilating power. Even when no reflux takes place, stagnation and pressure in the ureter and pelvis may reach a point where further secretion of the kidney will be impossible. Since Bumpus has seen such a reflux in only 4 to 6 per cent of his cases, we must admit that a free passage between the bladder, ureter and pelvis does not always exist. He carried out his x-ray examinations on chronic cases only where the bladder elasticity had been already restored. I believe that in acute cases such a free passage actually occurs far more often than can be concluded from his observations.

There is no doubt that such a back pressure will severely damage the renal parenchyma either through distention or through ascending renal infection, and will bring on such feared accidents as renal hemorrhages, oliguria, pyelonephritis, anuria and septicemia. Of 71 patients reported by Creevy who died after catheterization in the presence of residual urine, death was due to renal infection in all but 5. So all the old observations concerning the fatal consequences of sudden decompression were correct, but not the understanding of the real cause.

Sixteen years of experience with sudden decompression have established the following method of treatment: When a patient comes to us with a chronically distended bladder, we never catheterize him at once but bring him into the hospital. We never treat him in our office or at his home but always in the hospital where, under supervision of a doctor or a well trained nurse, all the necessary measures will be taken to insure continuous drainage of the bladder after decompression.

If possible, before emptying the bladder, we perform a bilateral vasectomy in order to prevent epididymitis. Then a Tieman catheter, 17 or 18, is inserted into the bladder and kept in place with adhesive tape. A small glass tube connects the indwelling catheter with a long rubber tube dipping into a bottle standing on the floor beneath the bed. The indwelling catheter should never be put directly into a urinal between the legs as this does not insure asepsis and favors decomposition of the urine and crystallization through open air contact. The bottle on the floor contains an antiseptic solution. The lower end of the long rubber tube is fastened on to a glass tube dipping into the antiseptic solution. Thus a permanent slight suction is achieved and there will be no direct contact with air.

During the first 24 hours as much water as possible is given to the patient. The higher the patient's nonprotein nitrogen, the more water he will want. A minimum of 3000 to 4000 cc output should be attained, but I have had cases with 6000 to 7000 cc output. The higher the output of urine the quicker will be the improvement in the patient's condition. Thirst subsides and the non-protein nitrogen sinks rapidly.

If the patient cannot consume enough fluid orally, physiological salt solution mixed with glucose has to be given subcutaneously, by rectal dropping enema, or in very bad cases with uremia and vomiting, by venoclysis, the more so because a certain amount of salt is required in order to ensure the secretion of urine. Immediately after decompression I have never seen a dangerous sinking of the blood pressure, however, later on a close watch of the condition of the heart must be made because of the strain occasioned by the excessive water intake.

If no obstruction such as small blood clots or shifting of the catheter hinders the free escape of urine, bladder washings should be avoided. The well established drainage system should not be disturbed for the first 5 to 7 days. In this way the highest possible standard of sterility is maintained. After this lapse of time the renal function is usually so much improved that treatment with sulfa drugs can be started.

During the first few days following decompression, blood is sometimes found in the urine, but no serious hemorrhages take place. Submucous hemorrhages of the bladder sometimes occur. They may be generalized, when they are due to the spastic contractions of the detrusor muscle, or localized in the area abraded by the tip of the indwelling catheter. Sometimes small blood clots obstruct the catheter so that a constant watch of the outflow of urine must be maintained. I have never seen hemorrhages demanding aspiration of bloodclots.

Creevy reports hemorrhages in 53.8 per cent of 26 cases treated by sudden decompression and 48.5 per cent in 33 cases in which emptying was carried out gradually, so that the percentages are practically the same. Therefore, compression itself cannot be the cause of these hemorrhages and no such thing as a hemorrhage ex vacuo really exists. This is confirmed by several cases with bladders containing between 7000 to 14000 cc treated by sudden decompression, none of which developed subsequent hemorrhages.

Since I believe that all hemorrhages after decompression are submucous bleedings, I prescribe 0.15 gm. papaverin hydrochloride suppositories 3 to 4 times a day, in order to relax the bladder muscle as quickly as possible. Usually hemorrhage stops very soon. If the patient cannot endure the catheter, I do not hesitate to give him morphine or any other sedative during the first few days.

In cases where we have to perform cystotomy we proceed in exactly the same way. We usually do not carry out the typical suprapubic operation for such cases, but prefer the puncture method with a trocar according to the technique of Pflaumer (Nurnberg). This method saves the patient a lot of preoperative anxiety and operative shock, since it can be carried out within a few minutes on any ordinary office table. Moreover, the fistula will heal by itself in a few days after the suprapubic catheter has been removed following prostatic resection.

SUMMARY AND CONCLUSIONS

Sudden and complete decompression of the distended bladder can be carried out without danger, provided certain rules are strictly observed. Acute and complete emptying has great advantages over the old method of slow and gradual decompression.

The reasons why it used to be looked upon as being dangerous are discussed at length as well as the measures to be taken in order to avoid complications.

REFERENCES

Brecher, E. and Chwalla, R.: Neues zur Therapie der Harnretention, etc., 31: 266, 1931.
Bumpus, H. C.: Urinary reflux. J. Urol. 12: 341, 1924.
Creevy, C. D.: Distention of the urinary bladder. Arch. Surg. 25: 356, 1932
Pflaumer, E.: Therapeutische Technik. Leipzig: Verlag G. Thieme, p. 771–830, 1942.
Rose, D. K.: Clinical application of bladder physiology. J. Urol., 26: 91, 1931.
Seifert, E.: Die Blasenblutung ex vacuo. Zentralbl. f. Chir., 67: 550, 1946.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

PERICYSTITIS: A CAUSE FOR THE RETENTION OF URINE FOLLOWING ABDOMINOPERINEAL PROCTOSIGMOIDECTOMY[1]

EDWARD W. CAMPBELL

The theory of neurogenic dysfunction as the only cause for retention of urine following abdominoperineal proctosigmoidectomy has not completely explained the varied aspects of this problem in the minds of many investigators. This is substantiated by the two schools of thought which have developed from the controversy.

Some authors consider nerve injury or destruction as the only cause for retention. Others consider an obstruction at the vesical outlet as an etiologic factor. The latter group approach the problem with a more open mind, and do not ignore the possibility of a neurogenic cause, but find it an infrequent occurrence.

Ewert's classification of causes, which follows, is exemplary of this attitude:

1) Pure detrusor paralysis from parasympathetic denervation.
    a) Mild form cystometrically evident in large numbers of patients the first week following operation.
    b) Severe form necessitating prolonged tidal drainage, present in a small number.
2) Mixed forms of detrusor paralysis in combination with
    a) Vesical neck obstruction.
    b) Almost complete loss of anatomical support and lack of fixation.
    c) Inherent resistance in the male urethra.
3) Vesical neck obstruction alone.

In the first part of this classification, a mild form of pure detrusor paralysis from parasympathetic denervation is mentioned which is cystometrically evident in a large number of patients the first week following operation. The only proof of neurogenicity of the lesion is the anatomic possibility of nerve distribution with regard to the operative procedure and a cystometric curve suggestive of a neurogenic bladder.

The question arises, can a cystometric curve suggestive of an atonic bladder be considered as unequivocal evidence of a neurogenic bladder? Collar and Eastman claim cystometrograms fail to substantiate the neurogenic hypothesis. Weyrauch, Lucia and Howard found a great variability among cystometrograms of normal, hyper- and hypotonic bladders. They have shown that numerous abnormal conditions may produce identical changes in the cystometrographic curve. We have found cystometry variable and not wholly reliable as a diagnostic procedure, but of great value for registering the progress of recovery.

The neurogenic hypothesis has been accepted by many for want of a better explanation. The anatomic relationship of the rectum and sigmoid to pelvic sympathetic and parasympathetic plexuses makes it difficult to conceive the removal of these organs without nerve injury. Yet the transient nature of vesical dysfunction in most cases following this operation is not comparable to the prolonged recovery following nerve injury from other causes. The rapid regeneration of postganglionic fibers has been offered as an explanation for the rapid recovery, but this does not explain the complete recovery of normal vesical function in 10 to 15 days, which is the rule, in the majority of patients, following rectosigmoid surgery.

---

[1] Read at annual meeting, American Association of Genito-Urinary Surgeons in Skytop, Pa., May 12, 1948.

Inadvertently, we have found a pathological process which can explain many of the variable aspects of early vesical dysfunction resulting from abdominoperineal proctosigmoidectomy. December 1947, we were required to do a cystotomy of a male patient 7 days following an abdominoperineal proctosigmoidectomy. The bladder was found to be distended and tense. The prevesical tissue was edematous, which state was thought to be due to posterior urethral trauma from ineffectual catheterization. However, the edema was found to extend down both lateral walls, and the perivesical tissue between the peritoneum and fundus of the bladder was also edematous.

The bladder wall was firm and of normal thickness. After opening the bladder it was necessary only to separate the wound edges to inspect the entire vesical cavity. The bladder wall was fixed and rigid due to extravesical inflammatory changes, so that its entire cavity could be inspected without retraction, as one might open and view the inside of a hollow rubber ball.

The patient had had no preoperative urinary symptoms of difficulty. He had had no unusual infection as the result of the rectal surgery, and had a minimal febrile reaction. As far as the rectal surgery was concerned the convalesence was uneventful except for urinary retention. There was no evidence of urinary extravasation which might have caused the pericystitis. It was an aseptic inflammatory reaction which was considered the result of trauma accompanying the abdominoperineal surgery.

The patient had had an inlying catheter for 1 week without evidence of marked infection. The catheter had become dislodged and attempts to reinsert the catheter had preceded cystotomy by 8 hours. It did not seem possible that the marked changes which we saw in and about the vesical wall could have occurred in this short period of time, as the result of catheter trauma or infection.

The rotund, fixed bladder wall surrounded by edematous areolar and adipose tissue presented a striking picture, the cause for which could not be ascribed to intraurethral or intracystic manipulation or infection. Extravesical infection was not evident as an extension from the perineal wound or extravasation from the urethra. Trauma from manipulation or retraction at the time of the abdominoperineal operation appeared to be the only cause.

Cystotomy in these patients is such a rare procedure that it makes visual observation of this pathological change in a series of patients impractical for proof of the hypothesis. Therefore, cystoscopic observation of the inflexibility of the vesical wall has been used to demonstrate the anatomic change in the bladder wall.

Since making this observation, we have had few opportunities to cystoscopically view the bladders of patients following abdominoperineal rectosigmoid surgery. We are not requested to see these patients until it has been found that they cannot void following removal of the catheter on the seventh day.

One male patient examined on the tenth postoperative day had a rigid and fixed posterior and lateral wall. The anterior wall to the air bubble moved freely on filling and emptying the bladder. Suprapubic pressure was then applied to forcibly express all the fluid from the bladder. The bladder did not collapse, so that it was possible to visualize the posterior wall of the fundus as well as most of the lateral walls. There were no marked mucosal or inflammatory changes. The bladder wall was fixed from an extravesical cause, not from an intramural or intravesical pathological change.

Two patients with prostatic hypertrophy examined on the fourteenth postoperative day had vesical walls which were freely movable on distention and emptying except for the posterior wall, which was completely immobile. These bladders could not be completely emptied with suprapubic pressure for the floor of the bladder could be distinctly visualized after forceful expression of the irrigating fluid. These patients were relieved of urinary retention by transurethral prostatic resection.

A fourth male patient seen 4 weeks following an abdominoperineal proctosigmoidectomy had a completely, but sluggish mobile vesical wall. His bladder could be emptied by suprapubic pressure with a cystoscope in the urethra. The bladder capacity was enormous and the detrusor muscles completely relaxed. There was a mild suggestion of a fibrous bar. Two transurethral resections for the removal of tissue from the entire circumference of the vesical outlet had not activated normal micturition. He has no desire to void and apparently no detrusor contractions with a moderately filled bladder. This man will undoubtedly have a prolonged period of retention such as one sees with traumatic cord bladder. This, I believe, is a true neurogenic bladder in contrast to the 3 previous cases.

It is within the realm of logical reasoning to conceive the possibility of a traumatic pericystitis resulting from the mechanics of a rectosigmoidectomy. The completely rigid vesical wall is incapable of contraction, and would cause an inability to void without a vesical outlet obstruction. Such a bladder would also give the prolonged low cystometric curve with minimal voluntary pressure elevation similar to that obtained with a true neurogenic bladder.

The striking predominance of urinary difficulties in the male patient stimulates further doubt as to its neurogenic origin. Seaman and Binning have suggested the protection of the bladder by the interposed uterus as the reason for the absence of female patients in their series. Marshall did not mention female patients in his discussion of this subject. Ewert reported 4.1 per cent of his cases with vesical dysfunction were female patients. McCrae has recently reported 46.1 per cent of his patients were females. This is exceedingly high as compared with other authors.

We have seen 2 female patients with vesical dysfunction both of whom had had a hysterectomy prior to rectosigmoid surgery. No reference could be found in the literature regarding the presence or absence of the uterus in the reported female patients who developed urinary retention following lower bowel surgery.

The intimate anatomic relationship of the bladder and rectum in the male would preclude more direct injury to the bladder, prostate and urethra than in the female with an interposed uterus and vagina. Removal of the uterus would expose the bladder to greater manipulation and trauma, thus creating an analagous situation to the male whereby a traumatic pericystitis may be produced.

Although the number of cases observed are too few to be conclusive, it can be concluded that traumatic aseptic pericystitis, as observed and described above in the postoperative case, can cause retention of urine without vesical outlet obstruction. The duration of the pathologic process would be comparatively short and commensurate with the principles of normal tissue and vascular repair. Such a pathologic process can explain many of the unanswered questions regarding early urinary retention following abdominoperineal rectosigmoidectomy.

1318 Medical Arts Bldg., Philadelphia 2, Pa.

REFERENCES

Collier, F. A. and Eastman, P. F.: Urinary retention following combined abdominoperineal resection. Surgery, 14: 223–228, 1943.
Ewert, E. E.: A comparative analysis of the urologic complications following large bowel surgery. J. Urol., 46: 764–776, 1941.
——: Transurethral resection for vesical neck obstruction following abdominoperineal surgery. Surg. Clin. N. Amer., 24: 588–592, 1944.
McCrae, L. E.: Management of [illegible] bdominoperineal procto- [illegible]
[illegible] stometrogram as a diag- [illegible] J. Urol., 51: 191–209, 1944.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

VESICO-INTESTINAL FISTULAS: REPORT OF TWO CASES OF FISTULA BETWEEN THE BLADDER AND LARGE INTESTINE CURED WITHOUT PRELIMINARY DIVERSION OF THE FECAL STREAM[1]

JOHN K. ORMOND

From the Henry Ford Hospital, Detroit, Mich.

Vesico-intestinal fistulas are of four kinds: 1) congenital (cloaca); 2) neoplastic (ulceration of intestinal carcinoma into the bladder, or vice versa); 3) inflammatory (diverticulitis, tuberculosis, etc.); 4) traumatic (fracture of pelvis, gunshots—operative accidents).

The records of the Henry Ford Hospital list 22 cases. Of these none were congenital; 11 were neoplastic; 8 were inflammatory; and 3 traumatic.

The treatment of congenital abnormalities is always difficult and time-consuming, and treatment of neoplastic fistulas discouraging and usually hopeless. The traumatic fistulas are the easiest to remedy; they sometimes heal spontaneously; and the inflammatory type presents the most interesting problems.

Inflammatory fistulas may not cause enough trouble to warrant operation. I have 1 patient, a woman, who has been under my observation for several years, who has a small vesico-intestinal fistula and occasionally passes gas, small seeds or small fecal particles with the urine. In spite of a mild chronic bladder infection she has so little inconvenience that she wants nothing done.

When repair of an inflammatory fistula becomes desirable, past experience has shown the advisability of a preliminary colostomy to permit subsidence of the inflammatory reaction in the bowel. This has reduced mortality and the incidence of recurrence.

There is a difference of opinion as to the preferred location of this colostomy; C. W. Mayo, for example, advises that it be made in the left lower quadrant; others advise a transverse colostomy high in the upper right quadrant. We favor the latter, since it leaves a clean field in the lower abdomen for the second operation.

With the advent of the newer drugs and other methods of treating and sterilizing the bowel, it seems possible that in selected cases, preliminary colostomy may be dispensed with.

I wish to present to you today, 2 instances in which vesico-intestinal fistulas have been cured by operation without diverting the fecal stream. One of these was traumatic in origin and most of that type do not require preliminary colostomy, but I am reporting it here because it presents other aspects of interest. The second case was of inflammatory origin.

On January 9, 1945 H. A. R., Henry Ford Hospital No. 432251, aged 73, was operated on for early carcinoma of the prostate, a radical perineal prostatoseminal vesiculectomy being done. Unfortunately in the course of the operation, the rectum was entered and a rectovesical fistula resulted.

---

[1] Read at annual meeting, American Association of Genito-Urinary Surgeons, Skytop, Pa., May 12, 1948.

The patient was very dissatisfied with his condition and wished that an attempt at repair be made before he returned home, so on March 27, 1945, seventy-seven days after the original operation, such an attempt was made, with the assistance and advice of Dr. Lawrence Fallis of the general surgical staff of our hospital. The plan of operation was essentially that devised by Drs. Hugh Young and Harvey Stone. Incision was made at the mucocutaneous junction of the anus and the mucous membrane of the rectum dissected up to, around, and above the fistula. Then the old perineal incision was reopened and the fistulous tract exposed and cut across. The opening into the bladder was inverted by means of catgut sutures. The rectal mucous membrane was then drawn down and cut off above the fistulous opening, and sutured to the anal skin margin. An effort was made to interpose muscle between the bladder and rectum, and a suprapubic cystostomy was done. Possibly it would have been wiser to have made a preliminary colostomy. At any rate the operation was unsuccessful, the vesicorectal fistula recurred or persisted, and he returned home with a cystostomy.

Fifteen months later he returned to the hospital for another attempt at repair. The cystostomy was functioning satisfactorily. A colostomy was not done, but he was prepared by the use of a Miller-Abbot tube, a bowel cleansing program and the use of sulfasuccidine.

After a few days of this regime, operation was performed in the following manner: Exposure was through the old perineal scar and was not difficult. There was no difficulty in finding the fistulous tract nor in cutting across it, thus separating the rectum from the bladder. We then had a small opening into the bladder slightly to the left of the midline in the line of the previous anastomosis between the urethra and bladder, and a much larger, irregular opening into the rectum. Neither was complicated by the presence of much scar or old inflammatory tissue. The opening into the bladder was inverted and reinverted with chromic catgut sutures, by means of Young's boomerang needle. Attention was then directed to the irregular tear in the rectum. The mucous membrane was closed with catgut Lembert sutures. Over this the muscular coat of the rectum was closed with interrupted silk sutures. Attempts were made to separate the two repaired areas as far as possible, and to interpose muscle tissue of the levator between them. Upon discharge 43 days postoperative, he was voiding normally and a few months later his urine was clear and there was no rectal leakage at all.

I do not know how much is to be learned from this case, but I believe three things may be emphasized: first, that the time interval between fistula formation and attempt at repair should not be too short in order that time be given for disappearance of the immediate inflammatory reaction; second, that the bowel should be sterilized as nearly as possible; and third, that silk or other nonabsorbable sutures should be used in the muscular wall of the bowel.

I believe that our first attempt at repair was made too soon after operation, and failed primarily because of the presence of unresolved inflammation.

Since this mishap we have prepared all our patients for radical perineal surgery by the use of sulfasuccidine or sulfathaladine and cleansing of the bowel.

A few years ago, I had the opportunity to see another man injure the rectum in the course of a radical prostatectomy. He repaired the rectum at the time of operation in the way I described—catgut for the mucous membrane and silk for the rectal musculature—and the healing in that instance was almost per primam—there was no rectal leakage at all. Recently, in performing a seminal vesiculectomy, I again had the misfortune to injure the rectum. I repaired it as described above and the wound healed with no rectal leakage.

The second case I wish to present is of a different nature. R. G., Henry Ford Hospital No. 509978, a 62 year old woman complaining of passing gas and food particles in the urine, was found to have a vesicosigmoidal fistula. Eleven days after admission, following preparation with penicillin and sulfacetamide, operation was performed, with the assistance and advice of Dr. Lawrence Fallis. A midline lower abdominal incision was made and the peritoneum opened. A loop of small bowel was found adherent to the posterior surface of the bladder, and the sigmoid was densely adherent to the left posterolateral wall of the bladder and the bowel wall at this point seemed considerably thickened. However, it was fairly readily mobilized and more detailed examination showed a diverticulum of the sigmoid attached to the bladder at the site of the fistula, for when it was dissected free the perforation was found. The bladder was opened and the indurated thickened area, evidently the site of the fistula, was excised and the bladder wall repaired about a Pezzer catheter. The diverticulum of the sigmoid was partially excised, and the sigmoidal defect brought about by this, closed with Lembert sutures. The anterior peritoneum was then closed in such a way as to extraperitonealize the sutured portion of the sigmoid. A drain was placed to the peritoneum at this point and an antiseptic pack was inserted down to the extraperitonealized portion of the sigmoid. A Miller-Abbott tube was passed in the operating room and allowed to remain in place for 5 days. The postoperative course was uneventful. Three and one-half weeks after operation the suprapubic wound was healed, she was voiding normally, and the urine was clear. Ten months later she remains well.

I bring this case to your attention because it seems possible that our newer methods of treatment of the bowel may, in selected instances, make it possible to cure vesico-intestinal fistulas of inflammatory origin, without preliminary colostomy, and thus shorten by a considerable period the necessary hospitalization and disability. In this connection I am privileged to cite a recent case of Drs. William Wishard and Willis Gatch of Indianapolis. They found a vesicosigmoidal fistula, and after preparation of the bowel by cleansing and antisepsis, operated without preliminary colostomy. In this case a portion of the sigmoid was resected and an anastomosis was done, and the patient, a woman of 75 years, did well.

This procedure would not be applicable in cases where there is extensive inflammatory reaction in the bowel, and I am not advocating the 1-stage operation for all or most cases of fistula due to diverticulitis. It is probably applicable in only selected cases where the inflamed area of bowel can all be removed, or where it can be mobilized sufficiently to be extraperitonealized. It is very important also that only healthy bowel come in contact with the bladder if recurrence is to be prevented.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

THE FEMALE URETHRA: A CLINICO-PATHOLOGICAL STUDY[1]

NORBORNE B. POWELL AND ELIZABETH B. POWELL

From the Departments of Urology and Pathology, Baylor University, College of Medicine, Houston, Texas

The problems relating to the female urethra have fascinated urologists, embryologists, and pathologists for many years. No attempt will be made to review the copious references on this subject. The excellent articles by Deter et al.[2], Van Duzen[3], Folsom and O'Brien[4, 5], Huffman[6], Johnson[7], and Evatt[8] have covered adequately the recent as well as the old literature. The preponderence of opinion as expressed by Renner[9], Folsom[10], Young[11], Huffman[6], Korenchevsky[12], Johnson[7], Beneventi[13], and others[14, 15, 16, 17, 18, 19], is to the effect that there are periurethral glands in the posterior urethra which often become infected and occasionally undergo hyperplasia. A contrary view is held by Cabot[20], MacKenzie et al.[21, 22], and Thompson[23]. Many writers have side-stepped the issue of the existence of true mucus-secreting acini in the posterior urethra and whether or not these should be designated "female prostate". However, these men do recognize that the posterior urethra is a frequent source of urological complaint and have contributed much to its clinical study.[24, 25, 26, 27, 28, 29, 30]

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 20, 1948.

[2] Deter, R. L., Caldwell, G. T. and Folsom, A. I.: A clinical and pathological study of the posterior female urethra. J. Urol., 55: 651–662, 1946.

[3] Van Duzen, R. E.: Glands of the female urethra. Urol. & Cutan. Rev., 48: 363–364, 1944.

[4] Folsom, A. I. and O'Brien, H. A.: The female urethra. J.A.M.A., 128: 408–414, 1945.

[5] Folsom, A. I. and O'Brien, H. A.: The female obstructing prostate. J.A.M.A., 121: 573–579, 1943.

[6] Huffman, J. W.: The development of the periurethral glands in the human female. Am. J. of Obs. & Gyn., 46: 773–785, 1943.

[7] Johnson, F. P.: Homologue of the prostate in the female. J. Urol., 8: 13–34, 1922.

[8] Evatt, E. J.: A contribution to the development of the prostate gland in the human female and a study of the homologues of the urethra and vagina of the sexes. J. Anat. & Physiol., 45: 122–130, 1910–1911.

[9] Renner, M. J.: The so-called female prostate and concretion formation in the female urethra. Surg., Gynec. & Obst., 52: 1087–1092, 1931.

[10] Folsom, A. I.: The female urethra. J.A.M.A., 97: 1345–1351, 1931.

[11] Young, H. H.: The pathology and treatment of obstructions at the vesical neck in women. J.A.M.A., 115: 2133–2136, 1940.

[12] Korenchevsky, V. and Dennison, M.: The histology of the sex organs of ovariectomised rats treated with male or female sex hormones alone or with both simultaneously. J. Path. & Bact., 42: 91–104, 1936.

[13] Beneventi, F. A.: Anatomy and histology of posterior urethra in newborn female. Surg., Gynec. & Obst., 76: 64–76, 1943.

[14] Lintgen, C. and Herbut, P. A.: A clinico-pathological study of 100 female urethras. J. Urol., 55: 298–305, 1946.

[15] Caldwell, G. T.: The glands of the female posterior urethra. Texas State J. Med., 36: 627–632, 1941.

[16] Spence, H. M.: Granular urethritis in women. J. Urol., 43: 199–203, 1940.

[17] Ormond, J. K.: Non-purulent urethritis in women. J. Urol., 33: 483–497, 1935.

[18] Hyams, J. A. and Weinberg, S. R.: Hyperplastic change at the vesical neck in the female. J. Urol., 51: 149–161, 1944.

[19] Caulk, J. R.: Contracture of vesical neck in the female. J. Urol., 6: 341–348, 1921.

[20] Cabot, H. and Shoemaker, R.: T[illegible] tion of infection of the urinary tract. [illegible]

[21] Mackenzie, D. W. and Seng, M. I [illegible] der and urethra. Canad. M.A.J., 40: 428–432, 1939.

[22] Mackenzie, D. W. and Beck, S.: A histopathological study of female bladder and urethra. J. Urol., 36: 414–436, 1936.

[23] Thompson, G. J.: Transurethral operations on women for relief of dysfunction of the vesical neck. J. Urol., 41: 349–359, 1939.

During 6 years of urological practice, one of us (N.B.P.) has been especially interested in the urethral syndrome in women. A total of 603 nonconsecutive private patients has been followed sufficiently to compile the data for this paper.

SYMPTOM COMPLEX

The urethral syndrome is protean in its manifestations and frequently flares up following pregnancy, a surgical procedure, or an illness which confines the patient to bed. An analysis of the most common symptoms will be presented along with their relative incidence (table 1).

TABLE 1. *Symptoms of 603 patients*

SYMPTOM	CASES	PER CENT
Bladder discomfort	582	96.5
Referred pain	362	60.0
Frequency	218	36.1
Burning	193	32.0
Urgency	171	28.3
Nocturia	151	25.0
Feeling of residual	56	9.3
Gross hematuria	52	8.6
Partial incontinence	46	7.6
Chills and fever	42	6.9
Urinary retention	36	5.9
Straining to urinate	33	5.4
Low grade fever	24	3.9
Dyspareunia	14	2.3
Enuresis as child	13	2.1

1,993 complaints in 603 female patients.

Bladder discomfort affected over 95 per cent of the cases and was characterized by variations in severity from a mild, almost unnoticed change in the normal urinary act to an excruciating consciousness of the urinary bladder. The onset was violently sudden or perhaps insidiously gradual over a period of

---

[24] Campbell, M. F.: Congenital bladder neck obstruction. South. M. J., 41: 99–107, 1948.

[25] Herbst, R. H. and Merricks, J. W.: Chronic primary diseases of lower female urinary tract. Med. Clinics North America, 25: 245–269, 1941.

[26] Beach, E. W.: Some observations of the female urethra. Urol. & Cutan. Rev., 38: 545–549, 1934.

[27] Hawley, H. C.: The female urethra and its relation to upper urinary tract infection. Proc. Roy. Soc. Med., 39: 741–748, 1946.

[28] Everett, H. S.: Urology in the female. Am. J. Surg., 52: 521–659, 1941.

[29] Spence, H. M. and Moore, H.: The female urethra in childhood. Texas State J. Med., 35: 234–238, 1939.

[30] Roen, P. R. and Stept, R. R.: Urethritis in girls. Am. J. Dis. Child., 72: 529–535, 1946.

weeks, months, or even years[31]. There often was improvement after an attack so that an individual was normal in between these episodes of "cystitis", "gravel", or "nervous bladder." In a high percentage of cases there was a history of one or more previous episodes of bladder discomfort.

Referred pain (60 per cent incidence) was an important though poorly appreciated factor in bringing the patient to the doctor.[10, 25, 32] This usually was a dull, indefinite suprapubic ache or pain in one or both groins, thighs, hips, loins, lumbosacral or sacroiliac areas. Occasionally it was severe, cramp-like, and alternated with knifelike cutting pains that radiated and simulated ureteral colic. When these colicky pains became bilateral, it simplified the diagnosis, for bilateral ureteral stones passing simultaneously are very rare indeed. Unilateral referred pain can be mistaken (and too often is) for intestinal or appendiceal; ureteral or renal; ovarian, tubal or uterine involvement. In this series 179 patients had backache, and approximately 80 per cent were diagnosed and relieved by urethral soundings plus digital massage of the piriformis muscle groups when pelvic myalgia also was present. Therefore, calibration of the urethra is essential in the differential diagnosis when pelvic pain or backache is present. As Folsom[32] put it so aptly: "Any pain within 2 feet of the female urethra which does not seem to be adequately accounted for by some definite pathology, should be suspected of being due to the urethra."

Frequency of urination was complained of by over 36 per cent of 603 patients. This frequency varied from a slight increase in the number of day voidings to almost constant going to and from the toilet. There often was associated strangury. A burning, aching pain during or following urination accounted for 1 out of 3 patients' symptoms. This dysuria usually was in direct ratio to the severity of the pathological process, though occasionally it was out of all proportion to the findings. Conversely, dysuria was a minimal or absent complaint in a few of the most severe cases.

Urgency of urination affected 28 per cent of the cases studied, and occasionally was severe enough to produce incontinence, so that the patient often mentioned shyly that she had a "weak bladder." This is in contradistinction to effort incontinence which usually is due to cystocele, though, of course, both can and often do co-exist. Varying degrees of nocturia were noted in 1 out of 4 of the 603 patients. Only 9 per cent of the women complained of a feeling of residual *urine after voiding, and as often as not, there was no appreciable residual found.* In the cases carrying the greatest amounts of residual, the patients often were surprised to find that they were not emptying their overworked bladders. Partial incontinence was obvious in 46 or 7.6 per cent of the cases. In about half of these, residual urine was the cause, while in the others inflammation, polyps, or bladder neck contractures accounted for this distressing symptom.

In 8.6 per cent of this series gross hematuria, usually painful, was the chief complaint. Only lower urinary tract hematuria is included. Thirty-five cases

---

[31] Addison, O.: Congenital obstruction of female urethra. Arch. Dis. of Childhood, 7: 25–28, 1932.

[32] Folsom, A. I. and Alexander, J. C.: Referred pain from the female urethra. J. Urol., 31: 731–739, 1934.

(5.9 per cent) had complete urinary retention, either acute or chronic. The youngest was a 2 year old white girl (case 2) with recurrent retention of 6 months' duration. The oldest was a 56 year old woman who had catheterized herself intermittently for 20 years.

Chills with high temperature (102–105 F.) was the initial finding in 42 cases (7 per cent). Complete urological investigation revealed only urethral and/or bladder neck disease in these women or female children as the etiological factor. Urethral sounding, antibiotics, and chemotherapy relieved the chills and fever. Occasionally, in chronic relapsing cases, upper urinary tract changes existed as demonstrated by x-ray and culture. However, most authorities consider these the unfortunate sequelae and not the cause of the lower urinary tract involvement.

Low grade fever in 24 women (4 per cent) previously had been diagnosed as fever of unknown origin. Often repeated elaborate laboratory tests and physical examinations had been done. A diagnosis of brucellosis, pulmonary tuberculosis, or foci of infection had been made without sufficient data. Four of these cases were in children in whom numerous urinalyses were reported negative, and thus the entire urinary tract was dismissed as a possible source of trouble. As Campbell[24, 33], Stevens[34], Spence[16, 29], Caulk[19],and others [30, 35] have demonstrated, regular passage of sounds through the urethra will cure these cases.

Straining to urinate, or increased difficulty in voiding was found in only 33 patients (5.4 per cent). This was a rather difficult symptom to evaluate, however, and one that many women neglected to mention in their histories, even though bladder trabeculations were present.

Dyspareunia was an infrequently recorded symptom. Only 14 women (2.3 per cent) confessed to painful coitus, though varying degrees of aversion, lack of orgasm, or real pain must be far more frequent than these data would indicate. A scarred, tender, inflamed urethra logically would be painful on intercourse, located as it is in the apex of the anterior vaginal vault. Frigidity surveys by gynecologists seldom take into consideration any possible urethral disease. With a sound in the urethra the pain produced by vaginal palpation of the instrument often will duplicate the vague indefinite discomfort that most women (and practically all gynecologists) associate with uterine malpositions or ovarian diseases. It is possible to relieve or cure these cases of dyspareunia rather easily by treating the urethra, to the great appreciation of both husband and wife.

In only 13 instances (2.6 per cent) were the patients able to remember childhood urinary difficulties, i.e. pyelitis or enuresis. Doubtlessly this figure is far too low, because memories of early trouble are easily forgotten and the diagnosis often incorrect. However, a history of retention, kidney infections, of bedwetting is of positive value.

Unfortunately, no data were kept regarding urinary tract involvements

---

[33] Campbell, M. F.: Pediatric Urology. New York: Macmillan, 1937, vol. I, chapter 3.

[34] Stevens, W. E.: Congenital obstructions of the female urethra. J.A.M.A., 106: 89–92, 1936.

[35] Walker-Smith, A. B.: Disorders of micturition in the female. M. J. Australia, 2: 516–519, 1946.

during pregnancy. It is believed, however, that there is a direct parallel between the pyelonephritis of pregnancy and the presence of urethral lesions.

FINDINGS

Panendoscopy was done in all cases and there was pathological narrowing of the urethra in a total of 263, or better than 43 per cent, of these cases (table 2). Eighty-one women had urethral strictures, as judged by calibration of the urethra with acorn-tipped bougies. A diagnosis of stricture was made in every case in which the urethra would not permit passage of a 20 F. instrument. A diagnosis of stenosis of the urethra (135 cases) was made when a narrowing of the entire urethra was found to a size 20 F. sound. There were 47 cases in which the urethral narrowing was confined to the distal segment of the urethra. After a meatotomy, the urethral lumen often was calibrated as normal.

Peri-urethritis was rather marked in 130 instances. It was found in almost every case of urethral or meatal stricture. In about 1 out of 3 of these cases of peri-urethritis, definite evidence was found of urethral diverticulum in various stages of development. However, with periodic passage of sounds only 2 cases required diverticulectomy.

TABLE 2. *Clinical diagnoses in 603 patients*

Meatal stricture	47
Urethral stricture	81
Urethral stenosis	135
Periurethritis	130
Urethral diverticulum	38
Urethral granulations	145
Urethral polyps	215
Urethral enfolds	53
Folsom female prostate	10
Trabeculations of bladder	9
Bladder diverticulum	2
Bladder neck contracture	42
Residual urine	26

Granulations of the urethra were found in 145 women, and 215 had polyps. "Enfolds" is a term coined[23] to designate the intraurethral bulging of the lateral and anterior walls of the urethra, usually most pronounced in the posterior portion. These enfolds were thought to be the cause of obstructing symptoms in 53 instances In 10 cases these urethral bulgings were definite enough clinically to diagnose the case as a "Folsom female prostate."

In 9 cases there were gross trabeculations with cellule formation, and in 2 cases cystograms demonstrated well developed bladder diverticula.

In 42 cases a well formed median bar, or bladder neck contracture was seen cystoscopically. Nine of these were in female infants or children and were considered to be congenital. Residual urine was found in 26 cases and varied from 1 to 27 ounces Almost invariably when the residual urine amounted to more than three ounces, the patients had developed frequency, nocturia, and/or infection as a presenting symptom (tables 3 and 4).

TABLE 3. *Etiological classification of urethral syndrome*

1. Urethral obstruction
   a. Meatal stricture
   b. Urethral stricture
   c. Urethral stenosis
   d. Urethral granulations
   e. Peri-urethral glandular hyperplasia (enfolds)
   f. Urethral tumors
      1. Polyps
      2. Caruncle
      3. Carcinoma
   g. Urethral diverticulum
2. Bladder neck obstruction
   a. Congenital
   b. Traumatic
   c. Inflammatory
   d. Post-irradiational
   e. Bladder neck tumors
3. Neurological involvement
   a. Central nervous system lesion
   b. Peripheral nerve lesion
4. Combination of above

TABLE 4. *Ages of 603 patients*

AGE GROUPS (IN YEARS)	CASES
4 mo.–12 mo.	2
1–10	9
11–15	2
16–20	30
21–30	111
31–40	162
41–50	135
51–60	63
61–70	29
71–80	17
81—Up	4
Not recorded	31

TREATMENT

In all of the 603 patients, office treatment was given a trial. If the individual responded to urethral dilations (up to 28–31 F.), instillations, sulfonamides, and sedation, then gradually treatments were spaced farther apart. Occasionally endoscopic application of 5–20 per cent silver nitrate was helpful when other local measures failed. Endoscopy was repeated in every instance before the patient was discharged.

Those refractory to office treatment were re-examined with special attention to the bladder neck and posterior urethra. If polyps were found and were not too numerous or too large, a gentle superficial fulguration of a small segment of urethra with a point-tipped electrode through the McCarthy panendoscope was done at 10–14 day intervals. Sixty-one patients were fulgurated one or more times in the office. Vigorous fulguration was not done, nor a wide area treated, because the secondary edema within 3–7 days produced difficulty in urinating and occasionally acute retention. (It is better to do too little than too much.) (See table 5.)

Those cases which were resistant to office treatment and fulgurations, and persisted in carrying a residual of over 3 ounces were resected transurethrally. This procedure was carried out in the office under local anesthesia on 14 women who had contracted bladder necks. Eleven were cured promptly. It was simple to cut through the mucosa of the bladder neck and submucosal ridge with a quick short stroke that produced minimal discomfort to the patient. Usually this cut was made at 6 o'clock (posteriorly). In the tight contractures, it was amazing to see the entire bladder neck relax and spring open with only one or two cuts. With a little experience one could tell if the procedure were sufficient or if more cutting were required. Vaginal palpation of the urethrovesicovaginal juncture obviated cutting into the vagina. Three of these 14 cases did not respond, and the patients were hospitalized for operation.

TABLE 5. *137 Operative procedures in 130 cases*

OFFICE	HOSPITAL	
T.U.F., 61 cases	T.U.F., 13 cases	Total: 74 cases
T.U.R., 14 cases	T.U.R., 49 Cases	Total: 63 cases
Total: 75 Cases	Total: 62 cases (47 sections available for pathological study)	Total T.U. procedures, 137

In this series there were 62 hospital patients who had 65 operations. Thirteen of these were fulgurations and 49 were resections of the bladder neck and posterior urethra under spinal or pentothal anesthesia. Forty-seven cases had sufficient tissue available for histological study. The 9 infants and children were done under general anesthesia.

CASE REPORTS

Case 1. Mrs. M. W., a 24 year old white school teacher, was seen in consultation because of severe colicky pain in the right lower abdomen and temperature of 101 F. of several hours' duration. On 3 occasions in the past she had experienced similar attacks. The first time, 4 years previously, in another state, she had negative cystoscopic and pyelographic studies, so that an appendectomy was done. A year later another episode of colicky pain, this time in the left lower abdomen, was accompanied by diarrhea. Again a negative report following cystoscopy and pyelograms led to an abdominal operation: the left ovary was resected and the uterus suspended. Six months later symptoms of right lower abdominal colicky pains, severe backache, and dysuria again led to cystoscopy and pyelograms: this time the right ovary was resected and the right tube removed. Postoperatively a series of monthly ureteral dilations was carried out for 1 year with improvement of bladder symptoms, backache, and lower abdominal pains. When the present illness developed, treatments had been discontinued for 6 months. Excretory and retrograde urograms were normal in every respect. Panendoscopy revealed a urethra and meatus tight to a 16 F. sound, and urethral granulations. A meatotomy was done and sounds that were passed reproduced the lower abdominal aching, the ureteral and renal colicky pains, and the suprapubic ache. Within a few hours of the first passage of sounds, her temperature reached 104.5 F. Urethral dilations for the past year have been continued every 3 to 4 weeks with complete relief of all symptoms for the first time in 4 years.

Case 2. In 1942 a 2 year old white girl, C. T., a doctor's daughter, had 3 episodes of urinary difficulty, each culminating in retention. A complete survey was reported as negative 2 days previously by a urologist in another city. When seen by me, the child was in retention, and catheterization yielded 12 ounces of urine. Subsequently, she was unable to urinate, so a catheter was left indwelling for 2 days. Neurological consultation was negative. She urinated easily thereafter and was discharged. Within 3 weeks acute retention recurred. Again an indwelling catheter relieved her and allowed easy urination for a few weeks. After this episode, the author suggested consultation. The child was taken to Duke Hospital, where Dr. John E. Dees fulgurated the bladder neck and advised urethral dilations for several weeks. A 5 year follow-up has shown a complete cure.

This case is reported to illustrate how a baffling problem of retention in a 2 year old child was handled successfully by the third urologist to see the patient. The author obviously neglected to re-examine the bladder and urethra and thereby missed a chance to obtain a dramatic cure by a simple procedure.

Case 3. Miss M. G., a 48 year old white spinster, developed cord changes from pernicious anemia of 20 years' duration. Neurological examination revealed marked spastic ataxia, exaggerated reflexes, and hypertonicity. Panendoscopy showed 5 ounces residual; a coarsely trabeculated, chronically inflamed bladder, marked collarette enfolding of the bladder neck into the posterior urethra and a contracted bladder neck. Three grams of tissue were removed at transurethral resection. On follow-up examination, the bladder emptied to less than 10 cc, and urination was about normal.

This case illustrates a combination of central nervous system involvement, perhaps peripheral nerve damage, and urethral changes that produced a mild degree of bladder failure. Operation corrected only the urethral and bladder neck factors yet allowed the bladder to compensate by reason of better sphincter-detrusor muscle balance.

PATHOLOGY

Tissue from 47 resected cases was available for study. Grossly the weight of the specimens varied from 0.5 gm. to 3.5 gm.

When possible, all available pieces of tissue were sectioned, but no serial sections were made from the blocks. Had this been done, more true periurethral mucus-secreting glands undoubtedly would have been found, and the per cent of line 7 of table 6 would have been raised appreciably.

Most of the urethras were lined by a squamous rather than a transitional type of epithelium (3:1), and erosions or superficial ulcerations occurred in 81 per cent of the cases. The submucosa was not entirely free of inflammatory reaction in any of our cases, which is contrary to the findings of other investigators[2, 14]. The inflammatory cells were mostly lymphocytes and plasma cells with a scattering of eosinophiles and neutrophiles. Definite lymphoid follicles were found in half of the cases and were so prominent in 6 that the histologic diagnosis of follicular urethritis was made. Submucosal edema and hyperemia were associated with the inflammatory reaction in 85 per cent of the cases, whereas fibromuscular hyperplasia was marked in only 40 per cent.

TABLE 6. *Histological findings in 47 transurethral resections*

Epithelial lining of urethral mucosa	Transitional—26% Squamous—74% Eroded or ulcerated—81%
Submucosal inflammation	Mild—21% Moderate—49% Severe—30%
Lymphoid nodules	49%
Submucosal edema and hyperemia	85%
Fibromuscular hyperplasia	40%
Presence of Brunn's nests or glands	74%
Periurethral glands (true prostatic)	With concretion— 10.6% (5) Without concretion—14.8% (7)

A most striking histological finding was the frequency of the presence of subepithelial cell groups commonly known as Brunn's nests. These were found in the superficial portion of the submucosa close to the epithelial lining of the urethra. All were composed of solid masses of transitional or squamous epithelial cells, many of which showed central cystic degeneration. However, the resulting gland-like spaces were lined by layers of transitional or squamous epithelium with perhaps a single layer of columnar epithelial cells around the lumen. These have been called prostatic glands by some observers[15] and have been photographed as such. However, their histologic appearance is identical

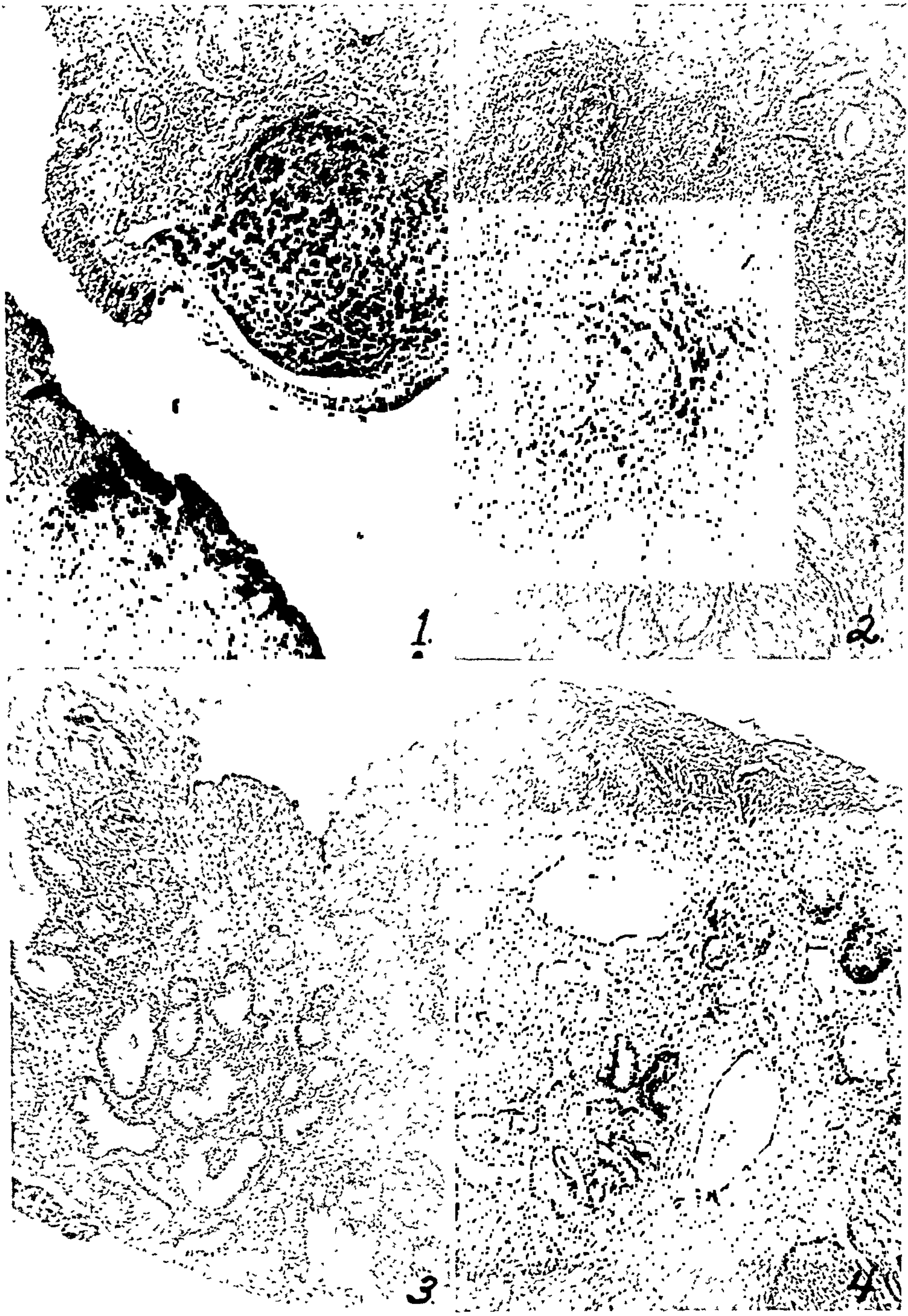


FIG. 1. *1*, upper left, A large hyperplastic lymphoid follicle bulging into lumen and covered by eroded transitional epithelium of urethra. *2*, upper right, Similar lymphoid follicle deeper in submucosa with a well developed germinal center and surrounded by Brunn's glands. *3*, lower left, In center of section is a large group of mucus-secreting acini lined by layers of columnar epithelium and identical histologically with male prostatic glands. *4*, lower right, Beneath hyperplastic squamous epithelium of urethra are numerous Brunn's nests, also composed of squamous epithelium and undergoing central cystic degeneration.

with the Brunn's glands seen in cystitis cystica and ureteritis cystica[36], and we agree with MacKenzie[21] that they are due to vacuolization and cystic degeneration of the Brunn's cell nests as a result of the inflammation and fibrosis in the submucosa of the urethra. Their presence in tissue sections warrants the histological diagnosis of urethritis cystica.

In 12 cases, we found what we believe to be true mucus-secreting acini in association with Brunn's glands. The former were found deeper in the submucosa, frequently in fibromuscular tissue. They were lined by one or more layers of columnar epithelium. The lumina contained either pale pink-staining material resembling mucus or deep reddish brown concretions. Histologically, these glands resembled those of the male prostate so strikingly that the tissue was identified as prostate by several qualified, unsuspecting pathologists. (See figure 1.)

We believe that true prostatic glands do occur in some female urethras but are far from an universal finding in obstructive lesions. There was absolutely no correlation between the histological presence of these prostatic glands and the severity of the clinical symptoms.

SUMMARY

The symptomatology of the urethral syndrome is protean in its manifestations.

Urethral pain can be referred to the pelvic organs, loins or legs, lumbar, renal, or ureteral areas.

Urethral obstructive symptoms in the female may mimic prostatism in the male.

Polyps, granulations, strictures, or enfolding collarettes of the posterior urethra may be responsible for the symptoms.

These symptoms usually respond to urethral soundings, instillations, fulgurations, or occasionally resections of the posterior urethra and bladder neck.

Transurethral fulguration was done in the office on 64 cases. It is a safe procedure which gives good results when the above mentioned methods have failed.

Transurethral resection was done in the office on 14 cases with 11 cures. It is an easy safe procedure when properly done.

Resistant cases should be resected transurethrally in the hospital and tissue removed for section.

In our series of 47 resected cases, in which tissue was available for study, 25 per cent showed true prostatic glands.

There was absolutely no correlation between the histological picture and the clinical history or findings.

A thorough appreciation of the urethral syndrome will help diagnose and relieve or cure many so-called "neurotic" women.

Hermann Professional Bldg., Houston 5, Texas.

---

[36] Friedman, N. B. and Ash, J. E.: Atlas of Genitourinary Pathology, Washington, D. C., 1946, p. 100.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

DISCUSSION

DR. HARRY M. SPENCE (Dallas, Texas): I rise to go along with my fellow countryman, Dr. Powell, who has beautifully brought to our attention a subject the practical importance of which is still not generally recognized.

After exposure to an adequate urological training, I, in company with all such newly-graduated residents, felt myself a surgical virtuoso adept at removing the prostate by all then-known methods. If I thought of the female urethra at all, it was as a channel to be traversed as rapidly as possible with a large Brown-Buerger cystoscope to investigate the bladder proper and the upper tract.

On entering practice, however, I was not deluged with prospective candidates for prostatectomy, but I was plagued by innumerable women with the syndrome of marked bladder symptoms, with normal urinalysis, or by recurrent cystitis for which I could find no cause.

I then fortunately came across Dr. John Ormond's classic paper entitled "Non-Purulent Urethritis in Women," in the *Journal of Urology*, May 1935. This solved many of my problems, and subsequent experience with the female urethra makes me in hearty accord with Dr. Powell.

It has been alleged that some have become over-enthusiastic in treating the female urethra, "hipped" on the subject, so to speak. This is entirely possible, just as it is potentially possible to abuse the use of prostatic massage, testosterone therapy, nephropexy, and so forth, all of which are valuable if properly used.

Suspecting, visualizing, treating, and getting results in diseases of the female urethra constitute a sound procedure.

For properly visualizing the female urethra and bladder neck, the panendoscope is superb, but the No. 16 Brown-Buerger concave (not convex) sheath, is likewise suitable if pulled down into the urethra.

Most cases respond to progressive dilatation at weekly intervals with the standard male sounds. Some require fulguration of granular areas and polypoid masses. Resection proper I have reserved for those with obstructive symptoms and demonstrable trabeculation of the bladder wall. I have never done a female bladder neck resection in the office.

Finally, granular urthritis occurs in childhood and many cases of common, persistent enuresis have been cured by conscientious and systematic urethral dilatation after psychogenic factors have been excluded or psychotherapy has been tried and found wanting.

DR. CHARLES PIERRE MATHÉ (San Francisco, Calif.): The Drs. Powell have just presented us with a most valuable contribution relating their wide experience in the clinicopathological study of the female urethra in 603 patients. They have emphasized the importance of using the panendoscope that permits one to uncover infectious lesions of the posterior urethra and vesical neck; infected mucous glands, polypi, etc., as well as obstructive lesions such as median bar, bladder neck contracture, and urethral stricture.

They have clearly demonstrated that, in many instances, urinary symptoms, referred pain, and overshadowing general symptoms are relieved by rather simple treatment consisting of dilatation of the urethra with sounds, topical instillations, destruction of the infected glandular structures by electrocoagulation, etc.

In the light of Dr. Lloyd Kindall's communication on allergy, one should consider this entity in the diagnosis and treatment of diseases of the female urethra.

Drs. Powell do not hesitate to employ resection of infected and obstructing tissue, particularly in those cases complicated by urinary retention. In addition to the female prostate, the obstructing contracting median bar and neurogenic bladder neck, I wish to call attention to a clinical entity which, in the female, unquestionably has been observed but sometimes misinterpreted; viz., hypertrophy of the vesical neck. I have seen a number of such cases presenting varying degrees of urinary retention due to hypertrophy of the muscle making up the vesical neck, in which there was no neurogenic disease. It is precisely the same pathological condition that was described by Marion in 1927, as congenital hypertrophy of the vesical neck, occurring in males.

A striking example of this disabling pathological condition was a female, aged 62, who, over a period of years, experienced increased difficulty in urination, culminating in complete urinary retention requiring intermittent catheterization. The obstructing hypertrophied vesical neck was resected in two sittings. Five grams of tissue were removed from all four quadrants, and pathological examination revealed hypertrophy of the bladder neck musculature. The patient is now able to empty her bladder completely.

The Drs. Powell have pointed out that simple lesions so common in the female urethra are often mistaken for pathological conditions in the uterus and adnexa, and in other abdominal organs. They are also confused with other diseases of the kidneys, ureters, and bladder. On the other hand, the infected mucous acini polypi and enfolding collarettes that one encounters in studying the vesical neck and posterior urethra with the cysto-urethroscope may point to trouble in the upper urinary tract.

We have repeatedly seen these glands about the bladder neck in patients presenting lesions of the kidney and ureter, such as pyelonephritis, ureteritis, ureteral stricture, nephrolithiasis, renal ptosis and torsion, hydronephrosis, renal tuberculosis, etc. *In my opinion, the presence of these infective glandular lesions calls for a complete study of the kidneys and ureter because, in some instances, infection comes from above and the inflammatory tumor is secondary to pathological processes in the kidneys and ureter.*

The Drs. Powell are to be congratulated on their timely contribution. Many urologists, in their zeal to uncover obscure diseases of the kidney and ureter, overlook lesions in the vesical neck and posterior urethra which are easily detected by employing the panendoscope and respond so readily to simple treatment.

DR. NORBORNE B. POWELL (Houston, Texas): I wish to thank Dr. Mathé and Dr. Spence for their kind remarks. I realized I might get "stepped on" a little bit by advocating transurethral bladder neck fulgurations and resections in the office. The office procedures often will require more than one operation in order to get the desired results.

The first attempt in the office was on a patient whose bladder neck had been resected in the hospital, and subsequently her symptoms were worse than prior to the operation. I had to do something and to my surprise and delight found that I could resect her bladder neck as described and the result was perfect.

I should like to review the pathological process. I think it is interesting.

(Dr. Powell read the section on the pathology, from the end of his paper.)

The Journal of Urology
Vol. 61, No. 3, March 1949
Printed in U.S.A.

RETROPUBIC PROSTATECTOMY: EARLY TECHNICAL DIFFICULTIES, REPORT OF REMOVAL OF GIANT PROSTATE[1]

SAMUEL K. BACON

From the Department of Surgery (Urology), University of Southern California School of Medicine, Los Angeles

The most useful purpose of retropubic prostatectomy is for complete excision of large or medium adenomatous hyperplasia, but this extravesical technique has been efficiently applied to all types of prostatic obstruction.

In this retropubic operation certain surgical difficulties and postoperative sequelae are minimized, while others are completely eliminated. However, the urologist must apply his thorough knowledge of anatomy and surgery. The surgical aspects of retropubic prostatectomy have been described, but are worthy of repetition and a review is given of the operation and useful technicalities which have since been developed.

Following anesthesia the bladder is lavaged and emptied. Starting just below the upper margin of the symphysis pubis, a longitudinal incision is made and developed to the retropubic space which is exposed by retraction. Prominent veins in the capsular area are underrun (with Millin's boomerang or a plain curved needle and chromic catgut No. 1) and ligated. Gently and lightly, gauze is packed into each lateral recess of the prostate.

Using a scalpel, a short transverse incision is made 1 cm. distal to the bladder neck through both capsules down to the prostate. The anterolateral plane of cleavage between the false capsule and adenoma is obtained by dissection with closed curved scissors. The prostate is enucleated from its apex by digital manipulation, turned upward through the capsular incision, grasped with a tenaculum, and removed under direct vision. Hemostasis is obtained by point fulguration.

After excising a posterior section of tissue from the vesical neck, a urethral catheter is introduced and guided into the bladder. The capsule is closed, if possible in 2 layers, using chromic No. 1 catgut and the boomerang, and the abdominal wound is repaired.

The significant problems in retropubic prostatectomy seem to be centered in one or two phases of the execution of the operation. Frequently the venous plexus of Santorini, and, rarely, an anomalous artery in the superficial region of the prostate may challenge the surgeon in his initial experience. This problem of hemostasis is promptly solved by judiciously utilizing ligation, clamping and fulguration.

When the retropubic space has been made accessible for careful inspection, any veins superficial to the prostatic capsule should be clamped with hemostats, divided with scissors, and diathermized through the instruments. The endopelvic fascia and its variable plexus of veins in close apposition to the true capsule of the prostate are revealed by displacing the adipose tissue with small sponges mounted on long forceps.

---

[1] Read at meeting of New York Society of the American Urological Association, New York, N. Y., March 11, 1948.

Millin has abandoned ligation of the central and lateral leashes of veins in the capsular area because of the frequency of annoying bleeding due to puncture. *He secures hemostasis after incision in the capsule by applying two special T-shaped angle forceps.* In the absence of these instruments, it is advisable to ligate prominent veins above and below the line of incision into the capsule. In *many* cases, it will be found that not a single vein requires ligation. After cautious insertion of the ligature needle, should it become evident that a vein has been punctured, the needle is slightly withdrawn and passed underneath the vessels. More frequently, rapid completion of the ligation will effect prompt hemostasis. Vessels encountered after incision in the capsule are grasped with Kocher forceps and fulgurated. Throughout the procedure an open-end suction is decidedly essential to keep the field of operation dry.

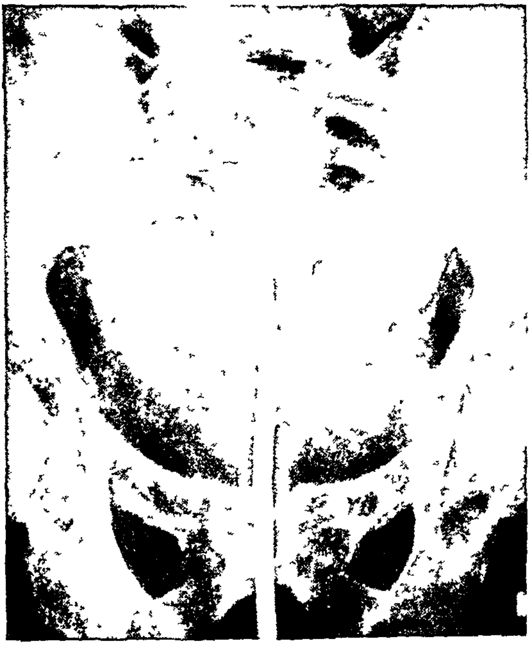


Fig. 1. Cystogram revealing enormous hypertrophy of prostate, occupying almost entire pelvis, displacing bladder upward (Courtesy of H. Spencer Hoyt)

After adenectomy the vesical neck is palpated and inspected thoroughly. Good visualization of this significant area is mandatory in order that an adequate section of the posterior lip may be excised with a pair of scissors, and Millin's "spreader," U.S.A. retractor or Babcock forceps will facilitate this important step. Although resection of this wedge is accomplished easily with a loop electrode, the use of the electrocautery, which devitalizes tissue, should be reduced to a minimum.

The following is a brief clinical history of a patient who had a giant adenomatous prostate, weighing 602 gm., which was removed by the retropubic route.

This case has not been published and is now reported through the courtesy of Dr. H. Spencer Hoyt.

CASE REPORT

The patient, aged 80, suffered from complete retention of urine during the past 20 years and had intermittently catheterized himself. Examination revealed the prostate in the suprapubic area to be about the size of a 3½–4 months pregnancy. After 3 weeks of hematuria, retropubic prostatectomy was carried out (figs. 1 and 2). Dr. Hoyt stated that "although this was my first retropubic operation, the degree of exposure and ease of removing this giant prostate weighing 602 gm., by this route, was highly gratifying." The patient made a good recovery and has had an excellent functional result.

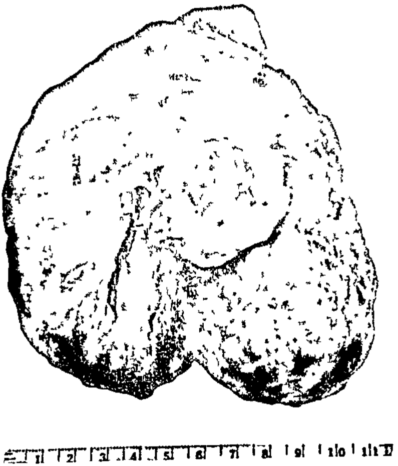


FIG 2 Gross specimen of giant prostate, weighing 602 gm., removed by retropubic technique. (Courtesy of H Spencer Hoyt.)

SUMMARY

Most useful purpose of retropubic prostatectomy is for complete excision of large or medium adenomatous prostatic hyperplasia.

Retropubic prostatectomy affords increased comfort during the comparatively short period of convalescence

Methods of eliminating difficulties encountered in the vascular area are described.

A previously unpublished case of giant prostate, weighing 602 gm., is described.

1680 N. Vine St., Hollywood 23, Calif.

REFERENCES

Bacon, S. K.: Retropubic prostatectomy: An extravesical technique; report of 32 cases. J. Urol., **59:** 376, 1948.

Bacon, S. K.: Discussion of retropubic prostatectomy by Terence Millin. J. Urol., **59:** 276, 1948.

Bacon, S. K.: Surgical technique of retropubic prostatectomy: An extravesical operation. Trans. South Central Section, A. U. A., 1947.

Millin, T.: Retropubic prostatectomy: New extravesical technique; report of 20 cases. Lancet, **2:** 693–696, 1945.

Millin, T.: Retropubic prostatectomy. Proc. Roy. Soc. Med., **39:** 327–338, 1946.

Millin, T.: Retropubic prostatectomy. J. Urol., **59:** 267, 1948.

Millin, T.: Retropubic Urinary Surgery. Baltimore: Williams and Wilkins, 1947.

THE JOURNAL OF UROLOGY
Vol 61, No 3, March 1949
Printed in U S A

RADICAL SURGERY IN PROSTATIC CARCINOMA[1]

FRANCIS PATTON TWINEM AND ALFONSO DAVALOS

From the Department of Urology, James Buchanan Brady Foundation, New York Hospital, New York, N. Y.

The purpose of this paper is simple; it is to urge radical operation in suitable cases of early prostatic carcinoma.

In the *Journal* of the *American Medical Association*, March 7, 1942, p. 855, in reply to a question, it is stated: "It is the opinion among urologists that once the diagnosis of carcinoma of the prostate has been made, it is technically impossible to do any sort of surgical procedure that would effect a cure. Once the diagnosis of carcinoma of the prostate has been definitely made, the condition is no longer surgical." We submit that this answer is not in accord with the facts. Radical operation is just as much indicated in suitable cases of carcinoma of the prostate as it is in suitable cases of carcinoma of the breast.

We have heard urologists with large practices state that they have never seen in their practice a case of prostatic cancer which they considered early enough to justify radical operation. This, we believe, simply means that they do not look diligently enough or that, in reality, they do not wish to perform this operation.

The word "radical" in the title of this paper is used in a general sense. Strictly speaking, we should distinguish the following types of perineal prostatectomy: 1) conservative, in which the prostate is enucleated from its capsule; 2) subtotal, in which the prostate and its capsule are removed but the seminal vesicles are left in; 3) total, in which the prostate, prostatic capsule, seminal vesicles and the ampullae of the vasa are removed; 4) radical, in which all the structures mentioned in the third category are removed and also part of the vesical neck is excised. For the purposes of this paper, categories 2, 3 and 4 are all grouped as radical. The cases used as a basis for this presentation were operated upon by several members of our staff and various degrees of radicality were employed.

In the light of recent evidence, cancer of the prostate is believed to be the most frequent type of internal malignancy found in the male. According to Moore and to Rich, prostatic carcinoma occurs in about 15 per cent of men beyond the age of 50 years. Professor Surraco of Montevideo, Uruguay, has done investigative work on this subject and gives, in a personal communication, the following as the incidence of carcinoma:

Age	*Incidence of Prostatic Cancer*
50–59	45%
60–69	55%
70–79	70%
80 and over	almost 100%

These figures are, of course, much higher than those usually given.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 20, 1948.

The U. S. Public Health Service gives the following incidence rate for prostatic cancer per 100,000 white population:

Age	*Incidence (cases first dia in the study year)*
45–54	9
55–64	48
65–74	200
75 and over	336

It is clear from the preceding tables that the incidence of prostatic cancer increases with advancing age. This, along with the increased life span at the present time and improved methods of diagnosis, probably account for the apparent increase in all forms of cancer in recent years.

Taking into consideration that probably at least 1 out of 7 men past 50 years of age has prostatic cancer, it is clear that many of these cases progress very slowly; otherwise, extensive metastasis and death from this condition would be more frequent than they are. However, they are of such frequency that we should be spurred on to endeavor to extirpate this disease, whenever possible, in its early stages.

Attention should be called to the fact that prostatic cancer, in about 75 per cent of cases, originates in the posterior lobe of the prostate, and that this lobe is not removed in any type of conservative prostatectomy; and it is not uncommon to find carcinoma in the posterior lobe or capsule some years after a conservative type of prostatic operation. We have had a number of such cases in our department.

What cases are suitable for radical removal? They should fulfill certain criteria; and this requires a particularly careful rectal examination. There should be no clinical evidence that the malignant process extends beyond the base of the seminal vesicles or into the membranous urethra. There should be no evidence of metastasis or extension beyond the capsule at any point. The serum acid phosphatase should be normal. The patient's general physical condition should be at least fairly good so that he has a reasonable life expectancy.

George G. Smith has advocated the radical removal of the prostate in cases in which it was quite certain that all the carcinoma could not be eradicated and felt that the patient's subsequent course justified this procedure.

With the presently available estrogenic substances, it is sometimes possible, by preliminary treatment, to render operable certain cases that would otherwise be considered inoperable.

In the present study there were 144 cases of prostatic carcinoma subjected to total prostatectomy. These operations were performed by various members of our staff, both attending and resident, and included both private and ward cases. In many cases no follow-up could be secured. However, we were able to follow up 84 of these cases.

MORTALITY

As to operative mortality, there were 13 deaths in the 144 cases, 9 per cent. The larger number of these deaths occurred in the earlier cases so that in the last 10 years there were only 3 operative deaths in 96 cases, a mortality rate of 3.1 per cent. With careful technique and the use of modern antibiotics a mortality rate of about 3 per cent should be secured.

Some of the patients in this series were operated upon primarily for relief of obstruction and did not fulfill the criteria for cases in which a cure could reasonably be expected. Of the 84 cases with follow-ups, 36 did not fulfill the previously mentioned criteria while 48 did comply reasonably well with these criteria.

Of the 36 not fulfilling the criteria of operability, 7 are now alive and 29 are dead. The average survival time of the 29 dead was 26 months. Of the 7 still alive, 6 were operated upon two or more years ago and their average survival time was 41 months. The average survival time for this entire group, excluding 1 case done only 6 months ago, is 28½ months (35 patients, 6 of whom are still alive).

Of these 36 patients who would ordinarily be classed as inoperable, 31 were operated upon 3 or more years ago with 10 (32 per cent) 3 year survivals. Of 18, operated upon 5 or more years ago, only 3 (17 per cent) survived 5 years and all of these died of carcinoma. Seven patients in this inoperable group are still alive at the following time (in months) postoperatively: 48, 48, 48, 42, 34, 24, 6.

Of the 48 patients fulfilling reasonably well the criteria for operability, 10 are dead and 38 are still alive. The 10 dead survived an average of 34 months. Six of these died in less than 3 years, 3 of cardiovascular disease, one with carcinoma of the bladder and 2 with metastatic carcinoma. One died at 3 years with metastasis. Two died of carcinoma at 4 years and one died at 5 years with no evidence of cancer.

Of the 38 patients in this group who are still alive only 5 have demonstrable carcinoma. Thus, of the 48 patients in this group, 10 are known to have shown subsequent evidence of metastasis or recurrence. Thirty-seven of the 48 were operated upon 3 or more years ago with 27 (73 per cent) 3 year survivals. Twenty-two of the 48 patients were operated upon 5 or more years ago with 12 (55 per cent) 5 year survivals.

The following table shows the survival time of these 5 year survivals:

5 yrs.	*6 yrs*	*7 yrs.*	*8 yrs*	*9 yrs*	*10 yrs.*
3	4	2	1	1	1

TECHNIQUE

Time permits only a brief description. We prefer the low curved incision, popularized by Belt, in which the fibers of the external anal sphincter are retracted anteriorly. The fibers of the median raphe are cut and the cleavage plan is followed along the longitudinal muscle fibers of the anterior rectal wall of the apex of the prostate. The fibers of the so-called "recto-urethralis" muscle are then pushed laterally or severed, and the levators well retracted laterally, exposing the fascia of Denonvilliers. The lateral aspects of the prostate are freed from surrounding tissue and the rectum is retracted well backward away from the seminal vesicles. A transverse incision is then made into the urethra at the apex of the prostate and a Markley tractor inserted through the tinence but he soon acquired complete and permanent urinary control. He left the hospital on the seventeenth postoperative day. Pathological examination of the prostate revealed nodular hyperplasia with one small area of tubular carcinoma. This patient should have a complete cure of his malignant process. It is the type of case for which all of us should be on the lookout, for only in this way will prostatic carcinoma cease to take its inevitable toll.

RÉSUMÉ

Cancer of the prostate is very common, occurring in at least one-seventh of all men past 50 years of age.

Cancer usually begins in the posterior lobe of the prostate where its presence can be detected by rectal examination. Every man 45 or more years of age should be examined annually by a urologist so that early cases of prostatic carcinoma may be detected and treated at a time when there is a chance for radical cure.

The incidence of prostatic cancer rises with advancing age.

The criteria for operability in this disease are given.

A series of 144 cases of prostatic cancer treated by radical surgery is reported with detailed follow-up study of 84 cases. In the cases fulfilling the criteria for operability, there were 55 per cent of 5 year survivals.

The technique of the operation is briefly described. There should be a low mortality of about 3 per cent and a good functional result is to be expected in the great majority of cases.

The value of orchiectomy and estrogens (including massive doses of stilbestrol) is discussed.

The significance of serum acid phosphatase determinations is outlined.

A summary of an illustrative case is given.

Total perineal prostatectomy is a rational surgical procedure and offers the only chance of cure in a condition otherwise certain to have a fatal outcome.

901 Lexington Ave., New York 21, N. Y.
525 E. 68th St., New York, N. Y.

REFERENCES

Alyea, E. P.: Early or late orchiectomy for carcinoma of prostate. J. Urol., **53:** 143, 1945.
Belt, E.: Radical perineal prostatectomy in early carcinoma of the prostate. J. Urol., **48:** 287, 1942.
Dean, A. L.: Carcinoma of prostate. Bull. N. Y. Acad. Med., **23:** 454, 1947.
Moore, R. A.: The morphology of small prostatic carcinoma. J. Urol., **33:** 224, 1935.
Paloma, A.: Carcinoma of the prostate gland. J. Urol., **53:** 166, 1945.
Rich, A. R.: On frequency of occurrence of occult carcinoma of prostate. J. Urol., **33:** 215, 1935.
Sheppard, M. D. Personal communication.
Smith, G. G.: Total perineal prostatectomy for carcinoma. J. Urol., **35:** 610, 1936.
U. S. Public Health Report, No. 2537.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

DISCUSSION

DR. CLYDE L. DEMING (New Haven, Conn.): I wish to thank Drs. Twinem and Davalos for the privilege of reading an advance copy of their paper. They have presented a relatively large number of cases of cancer of the prostate which they have endeavored to cure by radical perineal prostatectomy.

Sometimes large numbers are convincing. Jewett last week reported 221 cases so treated. The essayists, along with a few other urologists, are trying hard surgically to control prostatic cancer, while a larger number of surgeons are just treating this common cancer without regard for complete control of it.

The doctors have placed before you the criteria for radical operative procedures, which I heartily endorse. Their statistics show that the 5-year control of the favorable operable cases is between 50 per cent and 60 per cent, and for the so-called inoperable cases, 17 per cent. These figures are approximately the same as for other operators, but their statistics for the most part relate to patients who have been operated on less than 10 years. Many patients with cancer of the prostate live longer than 10 years without any treatment. Any statistics for control of prostatic cancer, to be of ultimate significance, should extend over at least a 10-year period after treatment is ended.

Since radical prostatectomy can be applied to a relatively small number of patients, hormonal therapy is being widely used. The transformation of an inoperable case to an operable one by preoperative estrogenic treatment may be adaptable to a few cases. We cannot guarantee that hormonal therapy will cure any prostatic cancer.

Our research embodying the heterologous growth of human prostatic cancer demonstrates pertinent facts: 1) that it is subject to a biochemical change in that it fails to produce the acid enzyme; 2) it becomes tolerant to estrogenic therapy; 3) the older it becomes, or the more generations it develops, the more independent it becomes, yet it does not change its morphology, and that is significant of a tremendous carcinomatous factor; and 4) the greatest effect from hormonal therapy should be anticipated from early treatment with large doses of estrogen.

Clinically this is true, and we are stymied in our expectations to control cancer of the prostate by estrogenic administration. We must make some new advances.

Perineal prostatic biopsies should be encouraged for all nodules in the prostate. Transurethral and suprapubic approaches fail to reach these areas, and needle biopsies are unsatisfactory in most clinics. The only sure control is total excision wherever the cancer is limited to the prostate.

Those who perform only transurethral resection cannot hope voluntarily to control cancer of the prostate, even if the case is one which satisfies the criteria for radical prostatectomy. The suprapubic prostatic surgeon is not much better off, because most of the prostatic cancers begin in the posterior lobe. While the retropubic surgeon may succeed in a total removal of a cancerous prostate occasionally, I would advise him to try the perineal route, as it lends itself to a more clearly defined dissection and a more readily made anastomosis of the urethra and bladder. Especially is this true when the whole bladder neck must be excised. The perineal route is the choice approach, and the technique can be accomplished without great effort. With modern chemotherapy one need not fear sepsis if the rectum should accidentally be opened. Sew up the rent and put in a rectal tube, and withhold food by mouth for a week.

I do not wish to relax on the integrity of good surgical technique, because of the availability of antibiotics. We must improve our surgery and do it better than ever before. A little experience in perineal surgery will give the operator confidence in preserving the external sphincter of the bladder and the maintenance of urinary control; however, I wish to urge the writers to continue their attempts to do a complete excision of the prostatic cancer wherever possible, until some investigator can show cause of complete control by some other means. Those of you who are perfectionists with the rectoscope please lay those instruments aside when you meet a prostatic cancer which is operable. Use instead a scalpel and go to work in the perineum.

(Slide) I want to show some slides of surgical specimens. This shows a nodule in the right lower corner of the section. Biopsy showed this was cancer and the total prostate was removed.

(Slide) I have been looking for a long time for primary cancer in the middle lobe. This is the only one which I have been able to demonstrate. Most of the middle lobe is benign overgrowth. There are, in the tip, carcinomatous changes.

(Slide) This is a total prostatectomy with a small cancerous nodule in the anterior lobe. There is none in the posterior lobe. The lateral lobes are benign overgrowth. It was the firmness of the capsule of the gland that led us to do a total prostatectomy. Though the biopsy did not show it, we felt there was cancer in it.

(Slide) This is another cross-section of a surgical specimen which shows cancer of the posterior and anterior lobes.

(Slide) This is a large tumor which is mostly benign but is generally infiltrated with malignant areas of carcinoma.

(Slide) This is a small prostate which was nodular and which you see shows rather nodular carcinomatous areas, but which shows also carcinoma outside of the prostatic cancer. There are some of these cases which the finger cannot detect.

I show these because I think they help us to decide how we shall improve the surgical procedure in these cases. Transurethral resection cannot reach the posterior lobes and cannot cure many of these cases.

In closing, again I commend the authors for their attempt to control their cancer cases by radical surgery, because it is the only way that we have to control prostatic cancer today, and those of you who for various reasons do not attempt the perineal route, may I urge you to do so, and assist the rest of us improve the treatment for cancer of the prostate.

Dr. Hugh J. Jewett (Baltimore, Md.): The problem simply stated is this: Will patients with early cancer of the prostate live just as long and just as comfortably without the radical operation as with it? Some believe they will and some believe they will not.

To answer this question we must do two things:

First, we must compare the 10-year survival rate in a group of patients subjected to the radical operation with that in a group treated by conservative methods, taking into account the operative mortality and the postoperative complications.

Second, we must record the actual design of the operation employed, so that we can recognize the superiority of one particular type of radical perineal prostatectomy.

Dr. Twinem and Dr. Davalos are to be commended for their diligent survey of the record at the New York Hospital. It is only by the publication of such records that the answers to the above questions can be found.

Forty-four years ago Dr. Hugh Young performed his first radical perineal prostatectomy for early cancer. The design of his operation was not hastily conceived. With a keen appreciation of the principal pathways by which carcinoma eventually spreads from the prostate, he emphasized the necessity for the excision of the bladder neck and the wide removal of the layer of fascia covering the seminal vesicles behind and the layer covering them in front, so that the vesicles are never exposed, but are removed with the specimen en bloc. The importance of this part of the procedure has not been fully recognized by a number of operators.

(Slide) This is the objective of Young's operation, indicated by the dotted lines.

(Slide) This shows a dissection of a total cystectomy specimen. The perivesical fascia comes down behind, and in front, fuses with the prostate, and encloses the prostate and vesicles within a common compartment.

(Slide) Cross-section of the seminal vesicles which have been removed by radical operation, showing the intact fascia behind and in front, enclosing carcinoma cells in the perivesicular tissues. We have never found carcinoma cells in the lumen of the seminal vesicles or vas deferens.

(Slide) High power of the previous section, showing carcinoma in the perivesicular tissues. Seventeen patients with carcinoma cells in the perivesicular tissues lived 5 years or longer without recurrence; 2 of these, 9 to 10 years; 2, over 10 years.

Even when the carcinoma seems to be confined to a circumscribed nodule lying within one lobe, there should be no feeling of security. Of 31 such cases in our series, only 5 were found microscopically to be strictly localized. In 26, the carcinoma had extended widely through the gland, and in 11 of these, tumor cells were present in the perivesicular tissues.

In our series of 190 cases of radical perineal prostatectomy for microscopically proved cancer at the Johns Hopkins Hospital, 132 were done prior to May 1, 1943, and have been followed; 39 per cent have lived 5 years or longer, and of those operated on prior to May 1, 1938, 19 per cent have lived 10 years or longer, without recurrence.

(Slide) This shows the survival after segregating those cases in which preoperative rectal examination disclosed gross evidence of extraprostatic extension. In the group showing no palpable evidence of extension, 28 per cent have lived 1 to 27 years without recurrence.

In the total group of 190 cases the operative mortality was 6.3 per cent. In the last 100 cases there have been 3 deaths, and in the last 50, none.

To date, Vest's method of vesico-urethral anastomosis has afforded the most satisfactory urinary control. Seventy-five per cent had perfect control, 13 per cent slight stress incontinence, and 12 per cent, poor control. We must now seek some way to reduce this last figure still further.

Those who claim that conservatively treated patients will do just as well through the years as those subjected to the radical operation will have to support their position by the publication of a comparable group of cases with microscopically proved cancer.

DR. WILLIAM P. HERBST, JR. (Washington, D. C.): I shall limit my discussion to the chemistry of the problem involved. The chemistry concerns not only the soil in which the cell grows, but the chemistry of the cell itself. Dr. Deming, I think, has contributed most constructively in demonstrating that the cell loses phosphatase on successive transplantation. This, so far as I know, is the only constructive data up to the present time in so far as the chemical composition of the cell is concerned. Dr. Rhoads, I am sure, impressed all of us yesterday with the profundity of the problem of the steroids but if you will just for a moment consider the steroids, consider the chemistry of the pancreas, consider the chemistry of the thyroid, and of the pituitary, consider the chemistry of the gonads—mix these all up, and I think you begin to have some slight comprehension of the complexity of the problem.

We have attempted to increase our expectancy to as great an extent as possible; to do that, we have juggled these chemical factors as expediently as possible, and it has resulted in this program: We do not introduce any chemical therapy until the patient is going down hill or is suffering from pain; obstruction is treated by resection. After resection, nothing is done. Castration is the first chemical procedure. After castration, nothing is done other than supportive measures. We give stilbestrol in the smallest dose possible, to accomplish any control. The dose of this is increased as necessary. In addition to that, when we lose control with stilbestrol, we have found that irradiation of the pituitary sometimes gives as long as a year's continued control.

DR. ROBERT GUTIERREZ (New York, N. Y.): Last year, I presented at a medical society in New York, an article entitled "New Horizons in the Surgical Management of Carcinoma of the Prostate Gland", which has not yet been published. I drew attention to the fact that since the introduction of hormone therapy in carcinoma of the prostate, there has been a radical change in the surgical management of this disease. Whereas the prostate tumor undergoes a marked metamorphosis under the influence of hormone therapy with or without castration, including reduction in the size of the tumor, and a softening of its stony hard consistency and relief of clinical as well as anatomic symptoms, radical surgery is nevertheless indicated in an effort not only to remove the cancerous tissue, but to offer the patient the best possible prospects for a permanent cure.

In the past, only 10 per cent of cases were operable and thus amenable to surgical cure, while now, following the administration of hormone therapy, or castration, inoperable cases can be rendered operable, in about eighty per cent of cases. This transformation is possible especially in the group of adenocarcinoma, which is, moreover, the type of tumor most commonly encountered.

(Slide) This slide serves to demonstrate the two types of carcinoma of the prostate, namely adenocarcinoma and scirrhous carcinoma. In the former, following hormone therapy cure may be obtained by carrying out total perineal prostatectomy, whereas the latter type, namely the scirrhous form or carcinoma which does not respond to hormone therapy or castration, remains inoperable and incurable. Fortunately this group represents only about 20 per cent of the total number of cases of carcinoma of the prostate. It appears, therefore, that we urologists must consider a new approach in the management of adenocarcinoma of the prostate gland. Many cases may be inoperable not only because of expansion of the carcinoma beyond the capsule of the gland, but also because of associated difficulties in surgical technique or obvious evidence of bony metastasis. Many of these cases have been subjected to transurethral resection of the prostate gland as a purely palliative measure to relieve obstruction. This operation offers no possibility of permanent cure, nor does hormone treatment or castration. It is imperative that the indications for radical perineal prostatectomy should be revised.

I have operated on 15 cases since the introduction of hormone therapy, and of this group of cases, most were considered inoperable when first seen. Some of these patients are still alive, 5 and 6 years after radical perineal prostatectomy, and apparently free from the disease. It is therefore of great importance to institute proper preliminary preparation of the patient with hormone therapy, so that the radical perineal operation may be performed as soon as it becomes possible.

(Slide) This slide shows a schematic presentation of the four types of radical perineal prostatectomy applicable for cure of cancer of the prostate, and which I have employed in a small series of cases, following preliminary hormone therapy. These four types of operation include 1) total perineal prostatectomy, i.e., removal of the prostate with its capsule, followed by anastomosis of the membranous portion of the urethra to the bladder neck; 2) the operation indicated when the cancerous process has extended beyond the capsule of the gland, including besides removal of the prostate and its capsule, as in the first type of operation, also the removal of the seminal vesicles and ampoule of the vas deferens. It is followed by the same type of anastomosis of the membranous urethra to the bladder neck. This second type of radical prostatoseminal vesiculectomy and ampulectomy is the one which I have most commonly employed 3) The third type of operation is the more radical intervention described by Hugh Young 44 years ago for cases in which the carcinomatous lesions involve the bladder neck; namely, total removal of the prostate with its capsule, the seminal vesicles and bladder neck. This operation should always be followed by proper anastomosis of the membranous urethra to the remaining portion of the trigone of the bladder. 4) The fourth type of operation is intended for more advanced cases, in which the carcinoma involves the floor or the lateral walls of the bladder. For this operation a preliminary diversion of the urinary stream by transplantation of the ureters into the bowel is necessary. A combined abdominoperineal cystectomy, prostatectomy and seminal vesiculectomy is then performed.

Any one of these four types of radical perineal prostatectomy is applicable in a well selected group of patients, and all of these radical procedures are facilitated by proper preliminary preparation of the patient with hormone therapy.

Results following this new method of approach seem more satisfactory, especially as regards the prospect of permanent cure, which cannot be obtained in this disease by any other method.

DR. ALFONSO DAVALOS (New York, N. Y.): I want to thank the discussers of this paper. There are just two things I would like to emphasize: 1) The great importance of early diagnosis has once more been demonstrated. This is one of the main aspects of the treatment of carcinoma of the prostate. 2) There is a growing awareness of the importance of accurate pathological examination of tissue obtained by biopsy, transurethral resection, or open operation. In order to detect these cancers in the early stage, when there is a chance of cure by radical surgery, serial sections of specimens obtained at operation are now being made routinely by many pathologists both in this country and abroad, notably by Dr. Gil Vernet of Barcelona, Spain, who has made thousands of sections over a period of at least 10 years.

THE JOURNAL OF UROLOGY
Vol 61, No 3, March 1949
Printed in U S A

CARCINOMA OF THE PROSTATE: A STATISTICAL STUDY AND EVALUATION OF ENDOCRINE THERAPY, WITH A PRELIMINARY REPORT ON AN ADDITIONAL METHOD OF TREATMENT

HARRY Q GAHAGAN AND J. L FISCHMAN

From the Tulane Urology Service, Charity Hospital of Louisiana, New Orleans

In the records of the Charity Hospital of Louisiana at New Orleans, 737 cases of carcinoma of the prostate were found from 1917 through 1946. Prior to the institution of endocrine therapy, which began late in 1941, there were 513 cases recorded. Since late in 1941, there have been 224 patients diagnosed as having carcinoma of the prostate who have received endocrine therapy; 118 of these were treated by orchiectomy and 106 were treated with stilbestrol. This study was undertaken in an endeavor to determine which form of therapy offered the most to a patient with carcinoma of the prostate.

The first 513 cases were interesting from the viewpoint of determining symptomatology, average age, and the pressing need to find a more satisfactory method of handling these patients. However, they were unsatisfactory for use as a control group because of the poor follow-up. Therefore, the authors are taking the liberty of using as the control for comparative purposes the excellent series presented by Nesbit and Plumb in 1946. This control group consisted of 795 cases of prostatic carcinoma which were treated by methods other than endocrine therapy. The graph for comparison of the death rates of the 3 groups (fig. 1) makes use of this control group. The average survival from diagnosis to death of Nesbit and Plumb's group was 21.2 months. In evaluating the treatment of carcinoma of the prostate by the use of endocrine therapy, either orchiectomy or stilbestrol, it is important to determine if there has been any change in the average survival period.

There have been 118 cases treated by orchiectomy. One hundred cases have been followed at least 1 year or to death. Eighteen patients failed to return to the clinic and could not be traced by correspondence, by the social service department, or in the vital statistics bureau. Of the one hundred cases followed, 51 or 51 per cent have died. Forty-nine patients or 49 per cent have lived 1 year or longer since the diagnosis of carcinoma of the prostate was made.

There have been 106 cases treated with stilbestrol. Seventy-two cases have been followed at least 1 year or to death. Thirty-four patients were lost to follow-up studies. Of the 72 cases followed, 35 or 49 per cent have died. Thirty-seven patients or 51 per cent have survived 1 year or longer.

To simplify presentation of survival data gained from this study, the material is gathered in self-explanatory groups and listed in outline form.

I. Longevity figures for entire endocrine series
    A. All cases living and dead

1 Number of cases	172
2 Total months survived	4519
3 Average months survived	26.3

B. All cases followed to death:
1. Number of cases.. 86
2. Total months survived....................................1820
3. Average months survived................................ 21.2

C. All cases living 1 year or more:
1. Number of cases.. 86
2. Total months survived....................................2693
3. Average months survived................................ 31.3

II. Longevity figures for orchiectomy series.

A. All cases living and dead:
1. Number of cases.. 100
2. Total months survived....................................3032
3. Average months survived................................ 30.3

B. All cases followed to death:
1. Number of cases.. 51
2. Total months survived....................................1221
3. Average months survived................................ 24.0

C. All cases living 1 year or more:
1. Number of cases.. 49
2. Total months survived....................................1811
3. Average months survived................................ 37.0

III. Longevity figures for stilbestrol series:

A. All cases living and dead:
1. Number of cases.. 72
2. Total months survived....................................1481
3. Average months survived................................ 20.5

B. All cases followed to death:
1. Number of cases.. 35
2. Total months survived.................................... 599
3. Average months survived................................ 17.1

C. All cases living 1 year or more:
1. Number of cases.. 37
2. Total months survived.................................... 882
3. Average months survived................................ 23.8

The longest survival was a patient who died 78 months after the diagnosis had been made and who was treated by orchiectomy. One other patient is still living 69 months since diagnosis was made and who also was treated by orchiectomy.

It will be observed that for the entire endocrine series (IA), the average months survived was 26.3 as compared to 21.2 months in the control group of untreated patients. Since half the patients of this endocrine series are still living, the average months survived will naturally increase. Therefore, it can be concluded that endocrine therapy increases the life expectancy in patients with carcinoma of the prostate. Since this is not a closed series the amount of increase in life expectancy cannot be calculated until the last patient has died.

By comparing the average months survived in the orchiectomy series (30.3) with the average months survived in the stilbestrol series (20.5) it would appear that orchiectomy offers these patients a longer period of survival. However, it must be borne in mind that in the class of patients seen in the Charity Hospital there is no assurance that all of them took the stilbestrol regularly as was prescribed. In addition, the percentage of satisfactory follow-ups in the stilbestrol series was lower than in the orchiectomy series. Therefore, it is not believed that any definite conclusions can be drawn here as to the relative merit of orchiectomy versus stilbestrol therapy.

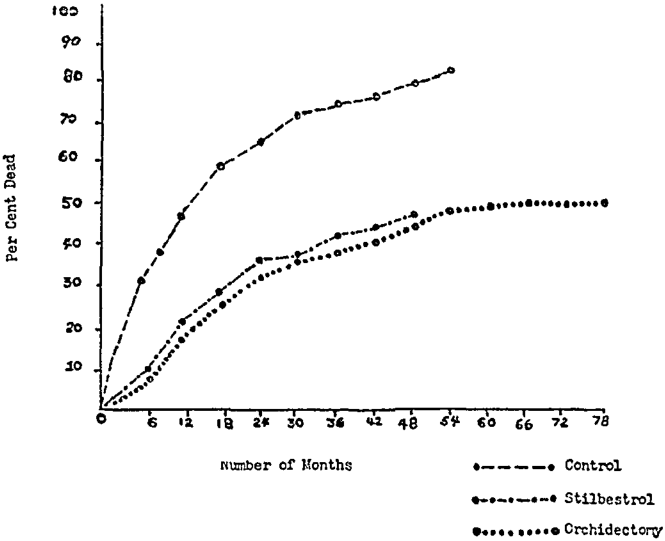


FIG. 1

A further comparison of groups is shown in figure 1. The death rates of Nesbit and Plumb's control group are compared with the author's orchiectomy and stilbestrol series.

In addition to the use of stilbestrol and orchiectomy in the treatment of carcinoma of the prostate, palliative deep x-ray irradiation over the sites of metastasis has been used. Dr. Manuel Garcia and Dr. Joseph Schlosser of the Department of Radiology suggested as an additional measure, the x-ray irradiation of the adrenals.[1] This was used in a few selected cases that had failed to respond to stilbestrol and orchiectomy. It was hoped that whatever androgenic function the adrenals had assumed would be eliminated.

There have been 10 cases treated by x-ray irradiation to the adrenals in addition to the use of stilbestrol and orchiectomy. All of these cases were far advanced. Three of the cases were markedly improved. One man with a destructive metastatic lesion of the fifth thoracic vertebra was living 37 months after treatment. He was paralyzed at the beginning of treatment but when last seen he was able to walk, although he still used his crutches for safety. Four patients failed to improve, but were virtually hopeless when therapy was started. Two patients failed to return for follow-up. One patient stated that he was improved but died 2 months after treatment. There have been no ill effects from this therapy.

---

[1] Dr. Manuel Garcia and Dr. Joseph Schlosser first used this additional therapeutic aid in February 1944.

One of the patients also has had irradiation of the pituitary with some slight improvement.

It is hoped that as more cases are treated with x-ray irradiation to the adrenals this measure can be more thoroughly evaluated. However, it would appear that x-ray irradiation to the adrenal might offer greater longevity and lower morbidity to some cases.

SUMMARY AND CONCLUSIONS

Endocrine therapy in the treatment of carcinoma of the prostate is definitely indicated as shown by the increase in longevity of cases so treated.

From this study, it would appear that orchiectomy offers more than stilbestrol in the treatment of carcinoma of the prostate. This is controversial as explained above.

X-ray therapy to the adrenals is offered as an additional therapeutic measure for further study and evaluation.

The authors wish to express their appreciation to Mr. Stayton Dempsey of the record library for his invaluable assistance in the collection of this material.

REFERENCE

Nesbit, R. M. and Plumb, M. D.: Prostatic carcinoma. Surgery, 20: 263–272, 1946.

The Journal of Urology
Vol 61, No 3 March 1949
Printed in U S A

AN ANATOMIC STUDY OF THE EXTERNAL URETHRAL SPHINCTER IN RELATION TO PROSTATIC SURGERY

HARRY C ROLNICK AND FALK K ARNHEIM

From the Departments of Urology, Cook County and Michael Reese Hospitals, Chicago, Ill

One of the most distressing sequelae of prostatic surgery is urinary incontinence Partial incontinence occurs infrequently following suprapubic transvesical prostatectomy and complete incontinence is rare Both partial and complete incontinence occur more often after perineal prostatectomy Many urologists who are well versed in perineal prostatectomy often hesitate to do this operation because of the increased incidence of incontinence Although retropubic prostatectomy has only recently come into vogue, it is evident from a review of the literature and our own experience that incontinence is rare following this operation Incontinence may follow transurethral resection This is usually the result of faulty technique in which the external sphincter has been cut However, incontinence following transurethral electroresection may ensue without any actual cutting of the external sphincter The explanation of urinary incontinence following any of these methods is well recognized as that of disturbance of the function of the external sphincter

The anatomy of the sphincter as described in the various anatomical texts is not clear It was felt that a study of this structure in relation to the prostatic urethra might be of help in explaining incontinence following prostatic surgery An investigation of the anatomy and the location of the external sphincter was, therefore, undertaken Particular interest was attached to its significance in relation to transurethral electroresection

Discussions of the nature of the bladder musculature, trigonal muscle and sphincter mechanisms have been long standing and divergent. The chief points of controversy have been the internal sphincter and the trigonal muscle Less emphasis has been placed on the external sphincter It is not to be concluded, however, that the anatomy of the external sphincter has, therefore, been settled

Present ideas of the vesical neck and external sphincter are derived chiefly from the work of Young and Wesson The external sphincter is described as beginning at the mesiolateral aspect of the vesical orifice Here the sphincter fibers are at first few and do not encircle the urethra They pass downward and backward, increasing in number and extending more posteriorly in a circular manner At a point opposite the apex of the prostate they are joined in a raphe forming a circular sheath around the urethra

McCrea later described the internal vesical orifice as consisting of two systems of encircling fibers The inner and more proximal was made up of smooth muscle fibers and was the internal sphincter mechanism The external sphincter was composed of the outer and more distal encircling fibers These sphincter mechanisms were said to be formed of both smooth and striated muscle fibers The former was derived from the posterior longitudinal bladder muscle fibers, the latter from an upward continuation of the urethral muscle

MATERIAL AND METHODS

The material for this study was taken from autopsies conducted at the Cook County Hospital on adult men, the vast majority of whose ages were over 50. The urogenital tract was removed en masse including the rectum and anus. The prostate and seminal vesicals were then dissected free from the rectum along the plane of Denonvilliers' fascia. For the purpose of this study the bladder was cut away through the trigone above the vesical neck and the urethra cut at varying levels as far as 4.5 cm. distal to the verumontanum. The anterior urethra was also cut away. Thus, the material consisted of a portion of the trigone, the bladder neck, the entire prostatic urethra and the membranous urethra. The urethra was then opened anteriorly along a line extending from the distal portion of the specimen through the vesical neck. The gross appearance of the specimen was described. Figure 1 illustrates the prepared specimen.

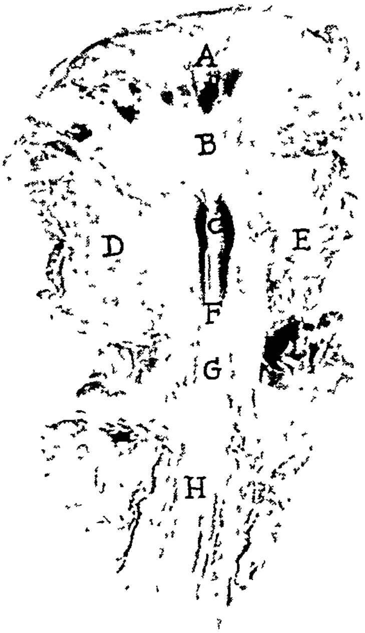


FIG. 1. The prepared specimen before sectioning: *A*, trigone: *B*, the bladder neck; *C*, verumontanum; *D* and *E*, lateral lobes of prostate; *F*, prostatic urethra; *G*, membranous urethra and *H*, anterior urethra.

No particular study of the anatomy of prostatic hypertrophy was made. This has been so adequately described by Randall. Some study was given to the vesical neck. We were particularly interested in the relation of the external sphincter to the prostate gland and its capsule. Careful measurements were therefore made of the length and depth of the prostatic urethra, both grossly and microscopically.

The verumontanum was taken as the starting point of all measurements. These were made from the veru proximally to the bladder neck and distally to the end of the gross specimen. Fifty-seven specimens were measured in the

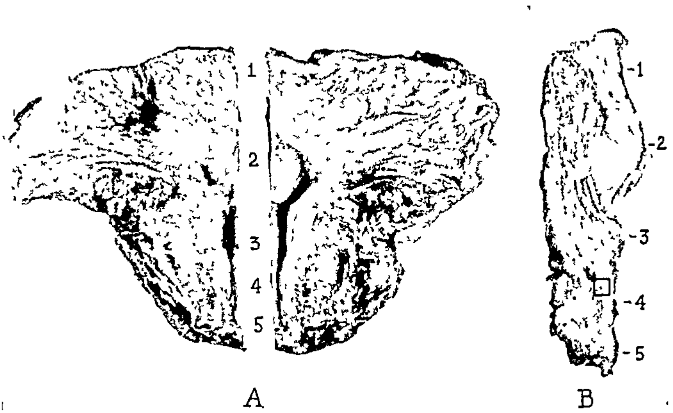


FIG. 2. Indicates how sagittal sections were taken through the verumontanum for microscopic sectioning. Block *B* extends from the bladder neck through the membranous urethra. *1*, Portion of the trigone *2*, Median lobe enlargement *3*, Verumontanum. *4*, Prostatic and *5*, Membranous urethra

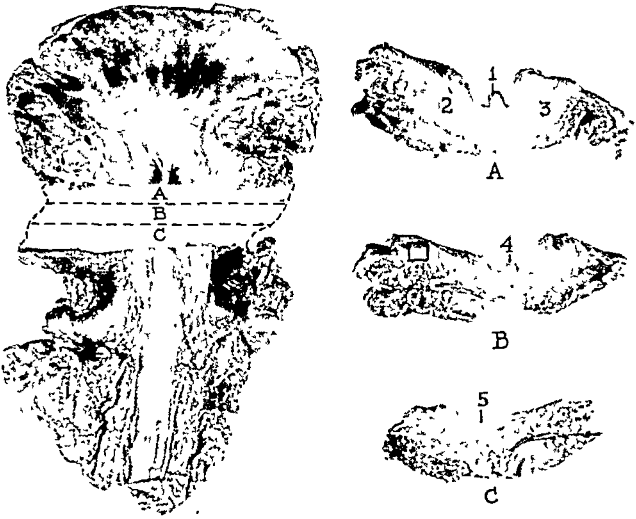


FIG. 3. Shows the way in which transverse sections were taken through the bladder neck, supramontane and inframontane areas for microscopic sectioning In this particular specimen, blocks *A*, *B*, and *C* were taken through the verumontanum and inframontane portion of the urethra. *1*, Verumontanum *2*, and *3*, Lateral lobes of prostate. *4*, and *5*, Crista urethralis

fresh state. They were then fixed in formalin solution and again measured in the fixed state. Thirty-five specimens were then cut sagitally through the center of the verumontanum and a block of tissue removed (fig. 2). Eight were cut transversely through the bladder neck and supramontane area. Nine were cut in the same manner through the inframontane area, apex of the prostate and the membranous urethra. These levels were approximately 4 mm. apart (fig. 3).

From these blocks, microscopic sections were made and stained with hematoxylin-eosin and Weigert's Van Gieson stains. Of those cut sagittally, 25 slides were selected as being most representative of the anatomy of the area. From these, the measurements of the distance of the verumontanum to the external sphincter were made microscopically. The figures obtained were corrected for any shrinkage that occurred during the processing of the microscopic sections. In all, 150 sections were made and studied chiefly for the location and nature of the external sphincter.

FINDINGS

It is necessary to consider certain gross features of the prostate gland, prostatic urethra and external sphincter in order to interpret the microscopic findings (fig. 4). It must be kept in mind that the urethra does not pass through the center of the gland. In a sagittal section, (fig. 4, *A*) two-thirds of the prostate is found posterior to the urethra. It should be emphasized that the sphincter follows the plane of the urogenital diaphragm in which it is enclosed. This inclination is largely determined by that of the inferior rami of the pubis to which the diaphragm is attached. The external sphincter can be considered as consisting of two groups of fibers, an outer set and an inner set (fig. 4, *B*). The outermost fibers of the sphincter take origin from the inferior rami of the pubis. They pass across the urethra to unite with those of the opposite side behind the urethra in a median raphe. The innermost fibers completely encircle the urethra. The anatomical distribution of the outer fibers acts as a hammock for the prostate and membranous urethra. It is also to be noted that the muscular branch of the perineal nerve innervates the external sphincter. The perineal nerve is a branch of the pudendal and divides into a superficial and a deep branch. It is the deep branch which penetrates the urogenital diaphragm from behind and gives its muscular branch to the sphincter. The innervation of the sphincter is chiefly from its posterior aspect. This has been verified microscopically (fig. 5).

The histo-anatomy of the area and location of the sphincter are shown in the drawing (fig. 6). This is a diagrammatic representation based upon a careful study of 90 sagittal sections of the prostate through the verumontanum extending from the bladder neck to and beyond the external sphincter. Superiorly the three muscle groups of the bladder can be identified. The large smooth muscle bundles of the middle circular layer are cut transversely. On each side of this layer are the internal and external longitudinal layers of the bladder musculature. Beneath these bundles the prostate gland is found in close approximation. There is an intermingling of the smooth muscle fibers of the prostatic stroma with those of the bladder musculature. The prostate itself is composed of many tubo-alveolar glands in which frequent corpora amylacea are seen. In the region of the verumontanum, the prostatic ducts are seen streaming into this area. The stroma of the gland is composed of a variegated pattern of fibromuscular tissue. At the apex of the prostate, the capsule of the gland is distinct. Outside the capsule are the striated muscle bundles of the external sphincter. These bundles are cut transversely in a sagittal section. There is an intermingling

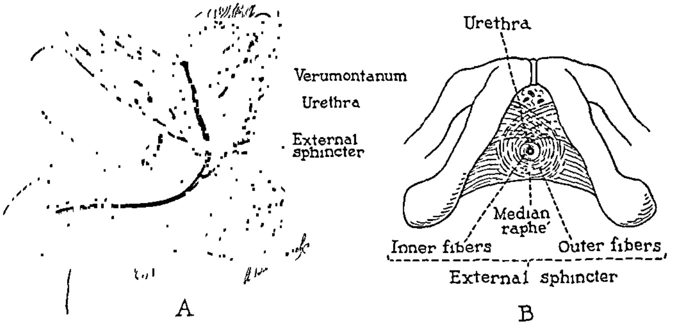


FIG. 4. *A*, Sagittal section through the bladder neck, prostate and external sphincter. The external sphincter is at a higher level anteriorally than posteriorally. *B*, Origin and insertion of the external sphincter. Note the division into outer and inner fibers.

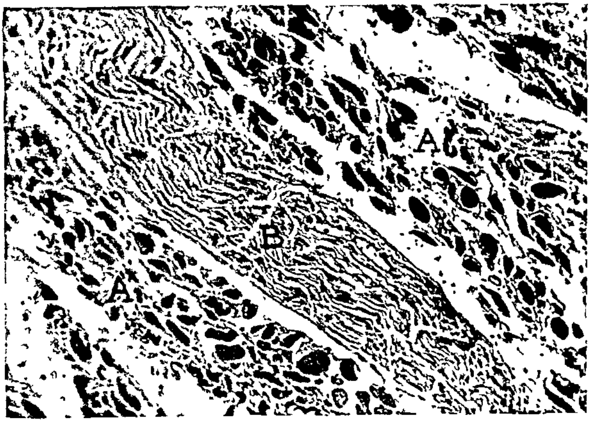


FIG. 5. Photomicrograph of a section taken from the posterior aspect of the external sphincter. *A*, shows the fibers of the sphincter cut transversely. *B*, is a nerve fiber. Many such fibers were seen throughout the slides

fresh state. They were then fixed in formalin solution and again measured in the fixed state. Thirty-five specimens were then cut sagitally through the center of the verumontanum and a block of tissue removed (fig. 2). Eight were cut transversely through the bladder neck and supramontane area. Nine were cut in the same manner through the inframontane area, apex of the prostate and the membranous urethra. These levels were approximately 4 mm. apart (fig. 3).

From these blocks, microscopic sections were made and stained with hematoxylin-eosin and Weigert's Van Gieson stains. Of those cut sagittally, 25 slides were selected as being most representative of the anatomy of the area. From these, the measurements of the distance of the verumontanum to the external sphincter were made microscopically. The figures obtained were corrected for any shrinkage that occurred during the processing of the microscopic sections. In all, 150 sections were made and studied chiefly for the location and nature of the external sphincter.

FINDINGS

It is necessary to consider certain gross features of the prostate gland, prostatic urethra and external sphincter in order to interpret the microscopic findings (fig. 4). It must be kept in mind that the urethra does not pass through the center of the gland. In a sagittal section, (fig. 4, *A*) two-thirds of the prostate is found posterior to the urethra. It should be emphasized that the sphincter follows the plane of the urogenital diaphragm in which it is enclosed. This inclination is largely determined by that of the inferior rami of the pubis to which the diaphragm is attached. The external sphincter can be considered as consisting of two groups of fibers, an outer set and an inner set (fig. 4, *B*). The outermost fibers of the sphincter take origin from the inferior rami of the pubis. They pass across the urethra to unite with those of the opposite side behind the urethra in a median raphe. The innermost fibers completely encircle the urethra. The anatomical distribution of the outer fibers acts as a hammock for the prostate and membranous urethra. It is also to be noted that the muscular branch of the perineal nerve innervates the external sphincter. The perineal nerve is a branch of the pudendal and divides into a superficial and a deep branch. It is the deep branch which penetrates the urogenital diaphragm from behind and gives its muscular branch to the sphincter. The innervation of the sphincter is chiefly from its posterior aspect. This has been verified microscopically (fig. 5).

The histo-anatomy of the area and location of the sphincter are shown in the drawing (fig. 6). This is a diagrammatic representation based upon a careful study of 90 sagittal sections of the prostate through the verumontanum extending from the bladder neck to and beyond the external sphincter. Superiorly the three muscle groups of the bladder can be identified. The large smooth muscle bundles of the middle circular layer are cut transversely. On each side of this layer are the internal and external longitudinal layers of the bladder musculature. Beneath these bundles the prostate gland is found in close approximation. There

The prostate and the external sphincter are separated from the urethral lumen by the submucosal structures belonging to the prostatic and membranous urethra. The urethra is lined by a transitional type of epithelium beneath which are seen smooth muscle, elastic and collagenous fibers. These run in a longitudinal and circular direction and form a fibroelastic muscular sheath for the prostatic and membranous urethra. In the prostatic urethra, the smooth muscle fibers blend with those of the prostatic stroma. In the membranous urethra they separate the external sphincter from the urethral lumen.

After the anatomical landmarks in the sections are identified, special relationships of the various structures can be determined. In the normal prostatic urethra, the average distance from the vesical neck to the center of the verumontanum is 1.6 cm. The average distance from the verumontanum to the external sphincter is 0.8 cm. The average length of the normal prostatic urethra is therefore 2.4 cm. The average depth of the external sphincter is found to be 0.2 cm beneath the urethral lumen (table 1).

TABLE 1. *Normal prostates*

DISTANCE FROM VERU TO VESICAL NECK	DISTANCE FROM VERU TO EXT SPHINCTER	LENGTH OF PROSTATIC URETHRA	DEPTH OF SPHINCTER (MEMBRANOUS URETHRA)
cm	*cm*	*cm*	*cm*
2.0	1.0	3.0	0.2
1.7	0.8	2.5	0.2
1.7	0.4	2.1	0.2
1.2	1.1	2.3	0.2
Av. 1.5	0.8	2.4	0.2

TABLE 2. *Lateral lobe enlargement*

DISTANCE FROM VERU TO VESICAL NECK	DISTANCE FROM VERU TO EXT SPHINCTER	LENGTH OF PROSTATIC URETHRA	DEPTH OF SPHINCTER (MEMBRANOUS URETHRA)
cm	*cm*	*cm*	*cm*
3.5	0.9	4.4	0.4
2.2	0.6	2.8	0.2
2.8	0.9	3.7	0.2
1.8	1.4	3.2	0.2
3.2	0.8	4.0	0.1
Av. 2.7	0.9	3.6	0.2

Certain changes in these measurements occur in benign prostatic hypertrophy (table 2). In the lateral lobe enlargements there is a considerable increase in the distance from the verumontanum to the vesical neck. Very little increase occurs in the distance from the verumontanum to the external sphincter, namely an average increase of 1 mm. These additions cause an overall increase in length of the prostatic urethra. There is no change in the cross sectional depth of the sphincter in the membranous urethra.

In the trilobar types of prostate, the distance from the verumontanum to the vesical neck is also increased as in lateral lobe enlargements. The total length of the urethra is still further increased due to a slight increase in the inframontane distance to the external sphincter. There is again no change in the depth of the sphincter (table 3).

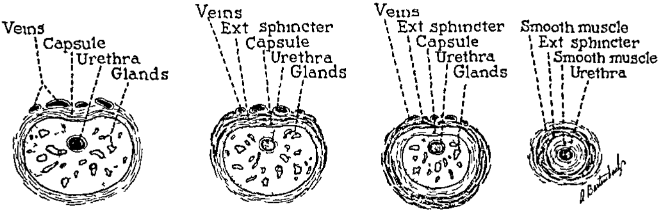
Special interest is attached to the inframontane distance to the external sphincter. The average distance of the verumontanum to the external sphincter for all our specimens is 0.9 cm. The shortest such distance occurs in a normal gland as was expected. It was 0.4 cm. The longest distance occurs in trilobar hypertrophy and is 1.6 cm.

TABLE 3. *Tri-lobar prostates*

DISTANCE FROM VERU TO VESICAL NECK	DISTANCE FROM VERU TO EXT SPHINCTER	LENGTH OF PROSTATIC URETHRA	DEPTH OF SPHINCTER (MEMBRANOUS URETHRA)
cm.	*cm.*	*cm.*	*cm.*
3.0	1.6	4.6	0.3
2.5	0.7	3.2	0.2
2.5	0.8	3.3	0.2
3.0	0.9	3.9	0.3
3.0	1.3	4.3	0.2
3.0	1.0	4.0	0.1
2.4	1.0	3.4	0.3
2.5	1.2	3.7	0.3
3.0	1.2	4.2	0.3
1.7	1.2	2.9	0.3
3.6	1.0	4.6	0.2
2.0	1.1	3.1	0.2
3.0	0.7	3.7	0.2
3.0	1.2	4.2	0.1
3.5	0.7	4.2	0.3
2.0	0.8	2.8	0.2
Av. 2.7	1.1	3.8	0.2

The drawings in figure 8 are an analysis of 30 sections taken transversely through five specimens. The levels begin at the vesical neck and extend as far distally as the anterior urethra. The striated fibers of the external sphincter begin to appear approximately 0.9 cm. distal to the verumontanum. Generally, they are first seen anteriorly on the roof. The muscle bundles are cut longitudinally and do not completely encircle the urethra. Adjacent to and blending with the innermost sphincter fibers is the prostatic capsule. The capsule surrounds the prostate which in turn encircles the urethra (fig. 9). As the levels descend, more of the sphincter is seen anteriorly and laterally; while at the lowest levels of the prostatic urethra, it appears posteriorly on the floor and thus, it completely encircles the prostate. There is always intervening prostatic tissue between the sphincter and urethral lumen until the membranous urethra is reached. Here, the thin layer of smooth muscle of the membranous urethra separates the sphincter from the lumen.

It is of particular interest to note that the external sphincter is present in the region of the distal prostatic urethra. It is separated from the urethra by intervening prostatic tissue and is present at a more proximal level on the roof than



4 mm distal to verumontanum

A

9 mm distal to verumontanum

B

Apex of prostate

C

Membranous urethra

D

Fig. 8. Series of drawings which illustrates the distribution of the external sphincter below the level of the verumont [illegible] by *A*. The external sphincter [illegible] encircle the apex of the prostat [illegible] are at the level of the membranous urethra

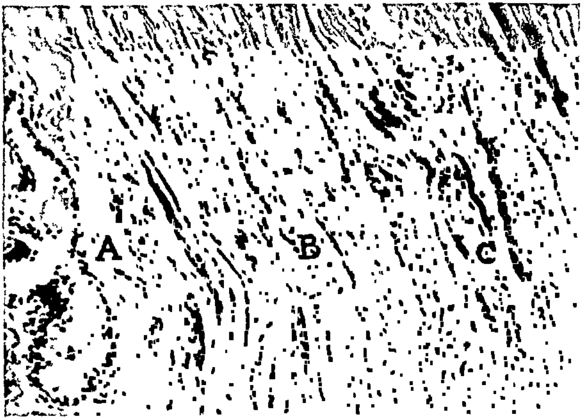


Fig. 9. Photomicrograph of a section [illegible] the prostate at its apex. The exact area is indicated by the [illegible] te is represented by *A*. Capsule of prostate is *B*. Fibers of [illegible] longitudinally and indicated by *C*. Note how the capsule intervenes between the sphincter and the prostate at this level

on the floor. The explanation of these findings is found in the anatomical distribution of the sphincter (fig. 4, *A*). The plane of the sphincter is not quite horizontal but is oblique, descending from anterior to posterior. The plane of the sections is perpendicular to the long axis of the prostatic urethra. This offers an explanation for the occurrence of the external sphincter fibers at a higher level anteriorly than posteriorly. Since the sphincter acts as a hammock for the membranous urethra and the apex of the prostate, it also envelops the prostate at its apex. This explains the finding of prostatic tissue between the urethra and the sphincter when viewed on transverse section.

RELATION TO PROSTATECTOMY

These anatomical observations on the external sphincter in the male are of interest in relation to the various techniques of prostatectomy. In view of the fact that all the operations on the prostate are intracapsular, except radical prostatectomy for carcinoma, it would seem that incontinence should not occur, for the external sphincter is extracapsular and should, therefore, not be directly traumatized in these operations.

Although relatively rare, some degree of incontinence may follow suprapubic transvesical prostatectomy. Even though the external sphincter is outside the capsule, it is in intimate relation to it at the apex of the prostate and can thus be traumatized when the enucleation is difficult. In these cases it is best to employ scissors to cut away some of the tissue rather than to possibly tear the capsule and the sphincter in the enucleation. Here as well as in perineal prostatectomy, the prolonged use of an inflated bag for hemostasis and prolonged tension on the bag may result in trauma to the sphincter. Persistent infection in the prostatic bed may later result in sclerosis of these tissues. In some cases, the sphincter may also be involved in chronic infection postoperatively. Carcinoma of the prostate, by infiltration, may invade the sphincter and thus in continence may follow prostatic surgery.

Perineal prostatectomy is also an intracapsular operation. The fact that incontinence is more likely to follow perineal prostatectomy is not due to actual injury to the sphincter. Two other factors are chiefly responsible 1) The nerve fibers innervating the external sphincter come in from the posterior aspect and the operative approach through this area may thus result in nerve injury. 2) The perineal muscles play some part in the act of micturition and urinary control, and may be damaged in the perineal approach to the prostate. Some urologists recommend a tight closure of the prostatic cavity following perineal prostatectomy by uniting the bladder neck to the membranous urethra. Incontinence may result here from the excessive traction on the external sphincter resulting from the sutures. The incision should be made high in the capsule at the bladder neck to avoid the external sphincter.

Retropubic prostatectomy is an operation similar to perineal prostatectomy. It is a direct approach to the prostate through an incision in the capsule except that it is done from above. It has certain advantages since the nerve supply to the prostate is chiefly on the posterior surface. The approach to the hypertrophied gland is away from its innervation. The enucleation of the prostate begins at the apex of the prostate and proceeds in a direction away from the sphincter, not toward it as in suprapubic transvesical prostatectomy. For these reasons, damage to the sphincter is even less likely than in the suprapubic or the perineal operations.

The findings in this investigation of the anatomy of the external sphincter were interpreted chiefly in the light of transurethral electroresection of the prostate. One of the most important considerations in this operation is the possible depth of thermal penetration. It is occasionally necessary to open the bladder after this operation because of extravasation due to perforation or for the control of persistent bleeding. The desiccation of tissues that occurs following electroresection can be observed and felt both in the prostatic bed and the bladder neck. The tissues are dry and leathery and the penetration is deep. This factor of thermal penetration must always be kept in mind. The sphincter is only 2 mm. in depth from the urethral lumen in the membranous urethra. It can, therefore, be injured without any actual cutting of the sphincter fibers.

It has been recognized clinically for some time that the level of the verumontanum is the safe distal limit to resection even though the sphincter is at some interval away from the verumontanum. Urologists are all mindful of the necessity of considering the level of the urethra at the verumontanum as the distal limit to any further removal of tissue. The average distance from the verumontanum to the external sphincter was 9 mm. on the floor of the urethra. It was found as close as 4 mm. and may be even closer in some cases of fibrosis and contracture of the bladder neck. Cutting distally to the verumontanum may be safe on an anatomical average, but may prove disastrous clinically since the verumontanum can be very close to the external sphincter. There should rarely be any indication for cutting distal to the verumontanum. It was pointed out that the enlargement in hypertrophy occurs chiefly in the supramontane area.

The danger of injuring the sphincter in transurethral resection when cutting on the roof must also be borne in mind. There is less prostatic tissue on the roof than on the floor of the urethra. The sphincter is, in addition, at a higher level anteriorly than posteriorly. Paradoxically, however, it has been found safer to cut on the roof than on the floor. Cutting into the sphincter anteriorly does not produce incontinence as readily as cutting the sphincter on the floor of the urethra. This may be due to the fact that the outer and inner fibers of the external sphincter are compressed into a small area posteriorly while anteriorly the outermost fibers swing out at some distance away from the gland to insert on the rami of the pubis. If these anatomical considerations are followed, incontinence should occur very infrequently following transurethral resection.

SUMMARY AND CONCLUSIONS

A histo-anatomical study of the external urethral sphincter has been made with special reference to incontinence following prostatic surgery.

Fifty-seven specimens consisting of the trigone, the bladder neck, and the entire prostatic and membranous urethra were prepared from autopsy material.

Accurate measurements were made of the length of the prostatic urethra both grossly and microscopically.

The location and structure of the external sphincter was determined from 150 microscopic sections. These were taken both sagittally and transversely through the specimens.

The apex of the prostate is enveloped by the external sphincter which acts as a hammock for this part of the gland.

The external sphincter follows the plane of the urogenital diaphragm. It is seen at a higher level anteriorly than posteriorly.

The external sphincter is in close approximation to the capsule of the prostate. There is an admixture of smooth muscle of the capsule and the striated muscle of the external sphincter at the junction of the two.

In the normal prostate the following average measurements were obtained:

	cm.
a. Verumontanum to vesical neck	1.6
b. Verumontanum to external sphincter	0.8
c. Vesical neck to external sphincter	2.4
d. Depth of sphincter in membranous urethra	0.2

The average distance from the verumontanum to the external sphincter for all specimens was 0.9 cm.

In prostatic hypertrophy the length of the prostatic urethra from the verumontanum to the vesical neck is greatly increased. The inframontane distance to the external sphincter is essentially unchanged. There is no alteration in the depth of the external sphincter in the membranous urethra.

The findings were interpreted in relation to possible urinary incontinence following suprapubic, perineal, retropubic and transurethral prostatectomies. Particular attention was given to the transurethral approach.

It is evident that since enucleation in the open operation is intracapsular, direct injury to the external sphincter should not occur in any of the procedures, for the sphincter is around and outside of the capsule. Other factors, such as increased tension and pressure on the sphincter by an hemostatic bag or by a pack tightly wedged in the prostatic urethra, are factors in injury to the sphincter. Secondary infection in the prostatic cavity with sclerosis of the sphincter may follow in some cases. Injury to the nerves and the muscles of the perineum are the chief cause of incontinence following perineal prostatectomy. Thermal penetration in electroresection is a large factor in possible incontinence following this procedure even though the external sphincter has not been cut.

REFERENCES

Bailey, F. R.: Textbook of Histology. Baltimore: Wm. Wood & Co., 1944, 11th ed.

Callander, C. L.: Surgical Anatomy. Philadelphia: W. B. Saunders Co., 1942, 2nd ed.

Cowdry, E. V.: Textbook of Histology. Philadelphia: Lea & Febiger, 1944, 3rd ed.

Cunningham, D. J.: Textbook of Anatomy. New York: Oxford University Press, 1943, 8th ed.

Goldstein, A. E. and Rubin, S. W.: Urinary incontinence following suprapubic prostatectomy. Urol. & Cutan. Rev., **50:** 664, 1947.

Grant, O. and Lich, R.: Consideration of the causes of incontinence, temporary and permanent, following perineal prostatectomy. J. Urol., **57:** 161, 1947.

Gray, H.: Anatomy of the Human Body. Philadelphia: Lea & Febiger, 1942, 24th ed.

Jackson, C. M.: Morris' Human Anatomy. Philadelphia: Blakiston, 1933, 9th ed.

Jordon, H. E.: Textbook of Histology. New York-London: Appleton Century, Inc., 1937, 7th ed.

Kalischer, O.: Die Urogenitalmusculatur des Darmes. Berlin, 1900.

Mac Leod, D.: Trigonal muscle with special reference to its composition and urinary function. Brit. J. Urol., **13:** 135, 1941.

Maximow, A. A. and Bloom, W.: Textbook of Histology. Philadelphia: W. B. Saunders Co., 1947, 4th ed.

McCrea, E D'A The musculature of the bladder Proc Royal Soc Med , **19** 35, 1926
Morrissey J H A new technique for perineal prostatectomy with preservation of the external sphincter Surg , Gynec & Obst **44** 671, 1927
Randall A Surgical Pathology of Prostatic Obstructions Baltimore Williams & Wilkins Co , 1931
Toldt, C Anatomischer Atlas Berlin Urban & Schwarzenberg 1919 10th ed
Thomson Walker, J W On the surgical anatomy of the prostate J Anat & Physiol , **40** 189, 1906
Van Duzen R E Anatomy of the prostate and vesical neck South M J **28** 785 1935
—— and Looney, W W Correlation of clinical and anatomical studies of the vesical neck South M J , **30** 436, 1937
Wesson, M B Anatomical embryological and physiological studies of the trigone and neck of the bladder J Urol **4** 279 1920
Young, H H and Wesson, M B The anatomy and surgery of the trigone Arch Surg **3** 1 1921
Young, H H and Macht, D A contribution to the physiology and pharmacology of the trigonum vesicae J Pharmacol & Exper Therap , **2** 329 1923

ADDITIONAL REFERENCES

Barnes, R W Endoscopic Prostatic Surgery St Louis C V Mosby, 1943
Bell Sir Charles Account of the muscles of the ureters and their effects on the irritable state of the bladder Trans Med Chir **3** 171 1812
Brenner, A The function of the vesical sphincter Ztschr f urol Chir **27** 241 1929
Eisendrath, D N and Rolnick H C Urology Philadelphia J B Lippincott & Co , 1943 4th ed
Flocks, R Repair following prostatic resection J Urol , **40** 208 1938
Goldstein, A E and Abeshouse, B S Postoperative urinary incontinence A review of literature and report of cases Arch Surg **21** 729, 1930
Gordon, G S The internal sphincter after prostatectomy Surg Gynec & Obst , **22** 620 1916
Langworthy O R Kolb L C , Lewis L G The Physiology of Micturition Baltimore Williams & Wilkins Co , 1940
Lowsley, O S The gross anatomy of the human prostate gland and contiguous structures *Surg , Gynec & Obst* **20** 183 1915
—— and Kirwin, T J Clinical Urology Baltimore Williams & Wilkins Co , 1944, 2nd ed
Millin T Retropubic Urinary Surgery Baltimore Williams & Wilkins, 1947
McLellan, F C The Neurogenic Bladder Springfield Charles C Thomas, 1939
Nesbit R M Transurethral Prostatectomy Springfield Charles C Thomas 1946
Rehfisch, E Ueber den mechanismus des harblasenverschlusses und harnentleerung Virchow's Arch f path Anat **150** 111 1897
Watson E M Status of the vesical sphincter after prostatectomy Surg , Gynec & Obst **29** 569 1919
Young H H and Davis D M Young's Practice of Urology Philadelphia W B Saunders Co 1926

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

RADICAL CURE OF VARICOCELE BY A NEW TECHNIQUE: PRELIMINARY REPORT

ALEJANDRO PALOMO

From the Department of Urology, San Carlos University, Guatemala City, Guatemala

Varicocele is an elongation, dilatation, and tortuosity of the veins of the pampiniform plexus. The spermatic vein is usually the only one affected, though the deferential or cremasteric may be involved. In 3 per cent of cases the condition is bilateral. Involvement of the right side only has not been recorded in medical literature, at least in the idiopathic form of varicocele.

Various degrees of dilatation of the veins may be encountered, even to the stage where there is a complete breakdown of the valves with atrophy and great thickening of the vessel's walls.

There are two kinds of varicoceles: 1) the idiopathic—the most common type, and 2) the symptomatic, due to kidney tumor, giant hydronephrosis, hepatic congestion, chronic constipation, muscular strain, et cetera. With the latter type we are not concerned in this paper.

PAMPINIFORM PLEXUS AND BLOOD SUPPLY OF THE TESTICLE

The pampiniform plexus is formed by 3 groups of veins: the cremasteric (posterior) group, the deferential (middle) group, and the spermatic (anterior) group—this last being usually the seat of varicocele. The left spermatic vein enters the renal vein at a right angle; the right one opens obliquely into the vena cava. The fact that 97 per cent of varicoceles occur on the left side suggests that the right-angled entry of the left spermatic vein into the renal vein, and the occasional absence of the valve on this side, predisposes of their formation.

The chief artery of the testicle is the internal spermatic, which arises from the aorta just below the renal arteries, sending a branch to the ureter as it crosses and passes, with the spermatic cord, through the inguinal canal to the testicle on the medial side of the body of the epididymis. Before entering the testicle, it sends a small branch to the globus major of the epididymis. Second in importance is the deferential artery, a branch of the inferior vesical (sometimes the superior vesical); this lies in intimate contact with the vas deferens until it reaches the epididymis, of which it supplies the body and tail. A third artery—the cremasteric, or funicular—which is a branch of the deep epigastric, runs in the external sheath of the cord to the lower pole of the testicle and epididymis.

Picque and Worms have shown that, in every case, there is an anastomosis between the 3 arteries. Sufficient blood supply to the testicle ought to be maintained if any 2 of these vessels are sacrificed. It is known that the internal spermatic artery may be severed without atrophy of the testicle resulting, but it does not seem probable that such would be the case if both the internal spermatic and deferential arteries are sacrificed—which is what happens in the well-known "accident" during operations for cryptorchism, hernial repair, and hydrocele, followed by atrophy of the testicle.

COMMENT

Many authors do not recommend surgical treatment of varicocele because they believe that such a procedure is not only unnecessary but unwise, especially in the case of the neurotic patient with neuralgia of the testicle. Nevertheless, many forms of treatment have been put forth. These include, in addition to psychotherapy and the use of a suspensory, injection (sclerosing) treatments, resection of the redundant scrotum, and open operations within the scrotum or the inguinal canal. Quite recently Drs. Ricardo Bernardi of Buenos Aires and Leander W. Riba of Chicago, Illinois published a method of treating varicocele by ligation of the spermatic veins.

The operation described above is, in our opinion, the simplest and easiest because it can be performed by almost any competent practitioner, with very few instruments, and in a few minutes. The patient need not be hospitalized.

Although 40 cases is a rather small series from which to draw deductions as to the efficacy of the method, we feel very optimistic because of our results thus far.

SUMMARY

The blood supply of the testicle is maintained after ligation of the spermatic artery.

A new technique for the radical cure of varicocele is discribed; in this, the spermatic vessels (artery and veins) are ligated and excised in a greatly simplified manner.

Forty consecutive cases in 38 patients, seen between March 1945 and March 1947 are reviewed. In 2 patients the condition was bilateral. All 38 patients were cured of their varicoceles, without atrophy of the testicle.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

ANURIA: REPORT OF TWENTY-SEVEN CASES[1]

JOHN K. ORMOND AND JOHN W. BEST
From the Henry Ford Hospital, Detroit, Michigan

In the dictionary anuria is defined as "complete suppression of urine." This is somewhat ambiguous, for the word "suppression" could mean either nonproduction of urine or nondelivery. So we reviewed the literature to find what in common usage, anuria means, and are using it in its commonly accepted sense; —namely, as that condition in which, after a period of inability to void, a catheter finds in the bladder either no urine at all, or only a very small amount. There is no clear line of demarcation between anuria and oliguria.

Urine is produced by filtration in the glomeruli followed by selective absorbtion and secretion in the tubules. The glomerular process is affected by 1) anything altering the composition or amount of the plasma; 2) anything altering the intra-glomerular blood pressure or 3) anything affecting the permeability of the glomerular capillaries. The tubular process is affected by 1) any damage to the lining cells, causing alteration in the ability to absorb or secrete—and at times causing leakage through the wall; 2) changes in intra-renal pressure—due to edema, etc; and 3) by endocrine disturbance; of the adrenals and pituitary particularly.

Taking the word "secretory" as including both the filtrative and secretory functions of the nephron, we can divide anuria into two general classes: obstructive or mechanical; and secretory. These in turn may be subdivided as follows:

1. Obstructive or mechanical:
   A) Tubular—due to deposition of crystals or casts: or compression caused by increased intrarenal pressure.
   B) Ureteropelvic—due to crystals, stones, stricture, tumor, or compression from the outside.
2. Secretory:
   A) Reflex—due to decrease in pulse pressure or effective blood pressure—or to shunting of the blood around the cortical glomeruli.
   B) Anemia, ischemia, dehydration.
   C) Glomerular disease; infections toxic or degenerative; acute or chronic.
   D) Tubular disease including lower nephron nephrosis.

And there may be combinations of these. Moreover, as will be shown later, some of these overlap and merge with one another.

In the fifth edition of French's *Index of Differential Diagnosis* appears the following incomplete list of causes of anuria:

A. Obstructive:

Calculus in kidney or ureter.
Vesical carcinoma involving both the ureteral orifices.
Uterine carcinoma infiltrating and obstructing both ureters.
Large pelvic or abdominal tumors obstructing both ureters.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

B. Nonobstructive:
- In renal disease:
  - Acute nephritis
  - Lardaceous kidneys
  - Tuberculosis of both kidneys
  - Polycystic disease of the kidneys
  - Suppurative pyelonephritis
- Other causes:
  - Acute ascending nephritis
  - Reflex, after operations or trauma, especially after operations on the lower urinary organs, after prostatectomy, or after perineal injury.
  - After the rapid emptying of an over-distended bladder.
  - In poisoning from mercury, lead, phosphorus, oxalic acid, cantharides, or turpentine.
  - In severe collapse, either from injury or in association with severe febrile illnesses, such as dysentry, cholera, yellow fever.
  - Hysteria.

Treatment, of course, is dependent on diagnosis; and cystoscopic examination is often necessary to differentiate between the secretory and obstructive types. This is well illustrated by 2 cases recently reported by one of us (and which will be reported briefly later on in this paper), in which anuria appeared suddenly, and with no apparent cause. Cystoscopy showed no urine in the bladder, but ureteral catheters found kidneys capable of normal secretion.

Treatment of the obstructive type consists primarily in the removal of the obstruction, and nothing further may be necessary. In the secretory type, the matter is not so simple. In glomerular disease, the anuria may be the terminal stage of a long process, in which case no treatment will avail; or it may be the result of an acute process, either alone, or superimposed on a chronic condition, in which case elimination of the cause of the acute process, plus supportive measures to preserve life until the reparative powers of the kidney have time to act, are necessary.

Reflex anuria includes two kinds of processes: 1) that due to a general lowering of the blood pressure (shock, for example), thus affecting glomerular function; and 2) according to Trueta, either to a local neurogenic narrowing of the renal artery; or a shunting of the renal circulation from the cortical to the medullary path, causing cortical ischemia and anoxia, and so affecting glomerular function.

Hemorrhage or dehydration affects the glomerular function by reduction in the amount of blood plasma circulating through them, or from lowered blood pressure.

The most interesting cases, as well as the most frequent and probably the most responsive to treatment, are the cases classed as "lower nephron nephrosis." This syndrome has been brought to our attention recently by Lucké, Thorn, Trueta, Corcoran and Page, and others and probably includes Van Slyke's "shock kidney." It is characterized clinically by anuria or oliguria, often increasing hypertension, and progressive azotemia. Initiating factors are many, and include shock, crush injuries, burns, intravenous hemolysis, sulfonamide sensitivity, toxemias of pregnancy, and organic and inorganic poisons. Pathologically, there is little disturbance to the glomeruli and proximal tubules, the striking renal lesions in all being degeneration and necrosis of the cells of the distal convoluted tubules and the descending loop of Henle, and heme casts in the lower nephron and collecting tubules.

Between those classed as reflex and those put in the category of lower nephron nephrosis (or the shock kidney of Van Slyke) there is only a time factor involved. If ischemia and anoxia persist beyond a certain point, focal necroses of the tubular cells occur, and it seems reasonable to suppose that the longer the period of anoxia, the more extensive the necrosis, possibly finally extending to the rest of the tubule, and even involving the glomerulus. So the distinction between the classes we have termed reflex, or due to hemorrhage and dehydration, and that termed lower nephron nephrosis, consists only in the fact that in the reflex type, the ischemia or hypotension is of brief duration, and is overcome before necrosis has taken place or before any important number of tubules have been affected.

In the past, these patients, in common with patients with other forms of anuria, have customarily been treated by the use of diuretics, and the pouring in of large quantities of fluids. Many patients have been killed by this treatment. "Fluids *were forced, and he was doing well, but, poor fellow, his heart gave out and he* died of pulmonary edema," has been a common verdict.

It was not realized that the trouble was due to damage, even to the point of necrosis, to certain cells in the tubules, and that only when these cells were regenerated, would the condition be remedied. Since the time required for regeneration varies, due probably to variation in the degree of damage, some recovered in spite of the treatment, early enough regeneration taking place to permit the patient to rid himself of the excess fluid before he drowned.

Rational treatment, then, in the light of our present knowledge, consists first in restoring as quickly as possible the blood volume, and in raising the blood pressure to reasonable levels. After this has been accomplished, no more fluids should be given than will replace the fluids lost through urine, stool, perspiration, respiration, vomiting, etc.; acidosis should be combated; and the electrolytes kept in balance. A high caloric, low protein diet should be given; and in long continued cases, with azotemia mounting to high levels, methods of abstracting from the blood some of the toxic products of metabolism may be useful in preserving life until the regenerative processes restore the natural excretory function of the kidney.

In this paper we are presenting 27 cases of anuria. There is room for a difference of opinion as to the classification of some of these—and we will endeavor to bring this out in our discussion of the individual cases.

A brief outline of each case is given. Some merit only passing mention, while others are discussed at length. It will be noted that we have classified none under the heading of tubular obstruction and that the largest number, 13, have been placed in the class of lower nephron nephrosis.

We have classified our cases as follows:

1. Obstructive or mechanical.
    A) Tubular
    B) Ureteropelvic
        1. Sulfa crystals in ureter, case 1

    2. Stone and solitary kidney, cases 2 and 3
    3. Bilateral strictures, case 4
    4. Metastatic carcinoma, cases 5, 6, 7
    5. Outside pressure, cases 8 and 9
2. Secretory.
  A) Reflex or shock, cases 10, 11, 12, 13
  B) Dehydration,
  C) Glomerular disease, case 14
  D) Lower nephron nephrosis, cases 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27

We will first outline and discuss cases 1 to 9, which are classed as obstructive or mechanical.

Case 1. A 42 year old woman was admitted with diabetic acidosis and pneumonia. She was given sulfadiazine for the penumonia and measures were taken to combat acidosis and diabetes. The next day sulfa crystals appeared in the urine and her urinary output dropped. Catheterization of the ureters was difficult because they were packed with crystals. Repeated lavage of the pelves cleared the pelvis of crystals, but she died on the seventh day. Autopsy showed that the crystaline, obstruction had been removed, but there were acute toxic myocarditis, pneumonia and pericarditis—as well as focal necroses in the spleen, liver and kidneys and wide spread parenchymatous degeneration of the renal epithelium. This patient was seen in 1940 and in view of the work of Lucké and Trueta, we believe this might well be classified also as an instance of lower nephron nephrosis. We have classified it as obstructive because of the proved presence of sulfa crystals in the ureters.

Case 2. A young man about 30 years old complained of anuria for 24 hours. A stone was found near the lower end of the left ureter, and cystoscopy showed no evidence of trigone or ureter on the right side. Fluids were forced. Four days later he died, with pulmonary edema, on the morning he was scheduled for operation. No autopsy was permitted. The treatment was at fault in 2 ways: operation was postponed, and fluids were forced.

Case 3. A young woman who had previously had one kidney removed, entered the hospital with anuria. Nephrostomy was done and she later passed a stone and recovered completely.

Case 4. A young woman, after a period of some months characterized by attacks of pain in both loins, suddenly was unable to pass any urine. When she presented herself for examination, there was no urine in the bladder, there were large masses palpable in the upper quadrants and flanks, and the nonprotein nitrogen was elevated. Bilateral nephrostomy, followed later by ureteropelvic plastic operations, remedied the situation and she lived several years, finally dying, however, of renal insufficiency. This is a very unusual condition and of considerable interest.

Cases 5, 6, and 7 are so similar that they are presented together in one paragraph. In each instance there was a history of previous carcinoma: breast, uterus and gastro-intestinal tract. Anuria developed and catheterization of ureters showed kidneys capable of function. Death occurred from other causes and autopsy showed involvement of the ureters in masses of metastatic tissue. Conditions like this are often encountered in the terminal stages of malignant disease of the pelvis, bladder and prostate. The 3 cases cites are unusual only in the suddenness of the onset of anuria and in the fact that metastases had not made their presence evident before.

Case 8. A man aged 43 was under the care of the Henry Ford Hospital for anemia and backache. Suddenly there was complete anuria, without any pain. Cystoscopy was done and catheters found urine in both renal pelves. Indwelling ureteral catheters permitted drainage of urine, but when the catheters were withdrawn, no urine reached the bladder. Abdominal exploration showed both ureters enveloped in a retroperitoneal inflammatory mass. They were freed and left free in the peritoneal cavity. Recovery was complete and he remains well 2 years later.

Case 9. A man aged 45 was admitted to the hospital because of sudden unheralded and complete anuria of 4 days' duration. Cystoscopic examination was done and catheters easily passed to the renal pelves, finding urine in each. When they were withdrawn no urine reached the bladder and they were later replaced. Bilateral nephrostomy was done. The ureters were dilated several times and the nephrostomies healed, but the urine remained infected in spite of repeated ureteral dilatations and the use of sulfa drug and penicillin. He became anemic and his renal function diminished. Finally, about 4 years after the episode of anuria, he entered the hospital and died of uremia. Autopsy showed both ureters enveloped in and compressed by an inflammatory retroperitoneal mass.

Discussion: These two are of great interest and have been reported previously by one of us. In both, anuria appeared out of a clear sky. In both, the obstruction was due to the envelopment of the ureters in an inflammatory retroperitoneal mass. The origin of this mass is not known in either instance. One suggestion is that it was a degenerating lipoma in each instance. We have been able to find no similar cases described in the literature. These 2 cases illustrate the extreme importance of cystoscopic examination in all instances of anuria not adequately explained. In the 1 case, No. 8, we have apparently achieved complete relief and it is probable that the same procedure would have relieved the other patient had we not unfortunately been able to dilate his ureters sufficiently to permit the nephrostomies to heal. For if the nephrostomies had not healed, we would undoubtedly have subjected him to abdominal exploration, found the condition, and freed the ureters as we did in case 8.

So much for the cases of obstructive anuria. We now take up those cases classed as secretory, cases 10 through 27.

Cases 10. A man aged 39 gave a history of severe suprapubic pain, gradual decrease in urinary output for 4 days, and complete anuria for 24 hours. On examination only $2\frac{1}{2}$ cc urine was found in the bladder, and the nonprotein nitrogen was 61.8. An x-ray showed a shadow suggestive of a stone in the region of the lower left ureter. Catheters were passed to each pelvis and a hydronephrotic drip occurred on the left and some urine drained from the right ureter. Indigo carmine appeared in 5 minutes on the right and in 12 on the left side. On the evening following cystoscopy, he began to void copiously, and the nonprotein nitrogen rapidly returned to normal. This is rather puzzling, but the history of anuria was very clear, and the blood nitrogen corroborated the history. We have classified this as a case of reflex anuria. We realize that a case could be made out for classification as obstructive.

Case 11. A 41 year old man had a urethral stricture dilated with filiform and follower. The filiform broke off and remained in the bladder. The stricture was then rapidly dilated and the filiform removed through a cystoscope. Following this he had a chill, his temperature rose to 106 degrees and he became comatose. There was anuria for 24 hours, in spite of an intake of 3750 cc. He then began to void and went on to complete recovery. We have classified this as reflex anuria.

Case 12. A man of 52 with hypertension had a cystoscopic examination because of microscopic hematuria. Normal pyelograms were obtained. He voided no urine for 2 days and none was found in his bladder; the nonprotein nitrogen rose to 70 mg. per cent. He was treated by renal diathermy and fluids forced to 3000 cc. He began to void at the end of 2 days and had no trouble thereafter. Subsequent investigations showed him to have chronic glomerular nephritis. A good case for the inclusion of this man under ureteral block could be made.

Case 13. A 42 year old woman had a diagnosis made of probable early carcinoma of the stomach, and with blood pressure of 140/80. In preparation for abdominal exploration, one afternoon she was given 300 cc of amigen solution slowly. This was followed by a severe chill and a rise in temperature to 105 F. 2 hours later. Her condition resembled shock, with cold and clammy extremities, cyanosis, rapid and thready pulse, and blood pressure of 56/30. The temperature became subnormal. She was given 1000 cc of 5 per cent glucose solution. Late that night she was given 1000 cc whole blood and was placed in an oxygen tent. The blood pressure the next morning was 60/40, the nonprotein nitrogen 55 mg. per cent, blood chlorides 493, hemoglobin 11.7 gm. and red blood cells 3,550,000. The first 24 hours there was 60 cc urine. On the second day the blood pressure rose to 96/62 and the urinary output increased and continued to increase, though the nonprotein nitrogen rose to 80 and did not fall to normal until 5 days later. This seems to be a case of suppression of urine secondary to the prolonged hypotension caused by a foreign protein reaction. It is interesting to speculate whether the ischemia and anoxia had persisted long enough to cause degeneration of the tubular cells. The duration was not long and we have not classed this as lower nephron nephrosis.

Case 14. A 52 year old woman, a known diabetic with hypertension, was admitted to the hospital in a stuporous condition with a history of anuria of 3 days' duration. Initial laboratory findings were as follows: Blood sugar 125; CO_2, 45.5; nonprotein nitrogen 103; diastase 16.5; hemoglobin 8.0; red blood cells 2,730,000; white blood cells 10,200.

She was treated at first by the intravenous administration of fluids containing glucose and sodium chloride. The next day, cystoscopy showed a normal bladder containing 5 cc urine; unobstructed ureters, nonsecreting kidneys, and no crystals were found. Catheters were left indwelling. The following day the nonprotein nitrogen had risen to 165, and peritoneal lavage and unilateral renal decapsulation was done. She was placed in oxygen and continuous peritoneal irrigation with Ringers lactate solution instituted. The following day she was mentally more clear, but the anuria persisted. The accompanying table shows how the blood chemistry readings were affected by peritoneal lavage. Three days later she expired rather suddenly, and autopsy showed advanced chronic and acute glomerulonephritis (fig. 1).

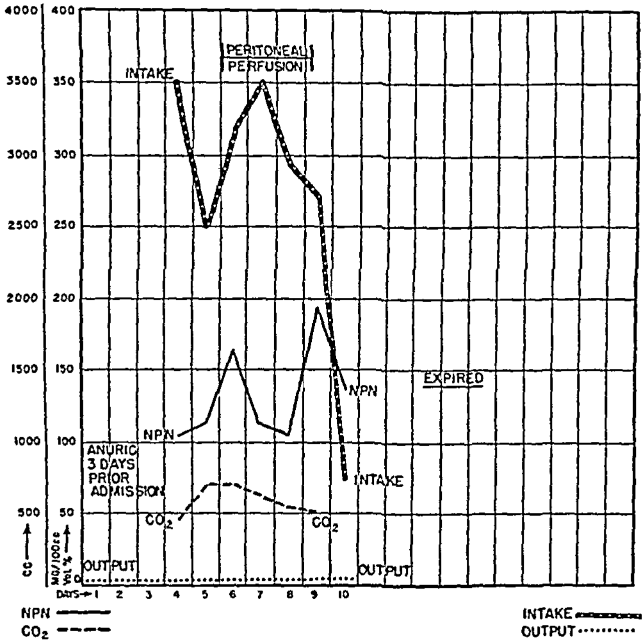


FIG. 1. Anuria-Terminal Nephritis #284244

DATE	BLOOD			PERFUSION FLUID
	NPN	CO_2	Cl	NPN
Adm. 4/30/47	103	45.5		
5/1/47	115			
5/2/47	165	70.5	333	
Perfusion				
5/3/47	115	58	390	A.M. 88 P.M. 115
5/4/47	100	63.2	400	68
5/5/47		52.6	427	84
5/6/47	135			83

Case 15. For the privelege of including this case in our list, we are indebted to Dr. W. G. Elliott and Dr. George A. DeJong of Detroit. A woman 37 years

old had had a posterior gastro-enterostomy and vagotomy for peptic ulcer. Her postoperative course was stormy and she was unable to retain fluids for several days, and became very dehydrated. In the first 9 days, the urinary output was very low, the measured output for the last 5 days of that period being only 255 cc, and the total output just about balanced the total intake. After this the urinary output steadily increased and the nonprotein nitrogen after rising for a day or so as high as 138, began to fall until it was 35 a week later. The blood chlorides had fallen to 284 on the day the urinary output began to rise, and rose steadily to normal. Clinically she had been in acidosis and was given lactate solution intravenously. At the turn in the tide, the CO_2 combining power of the blood was found to be elevated. For 46 hours, because of the elevation of the nonprotein nitrogen, her stomach was lavaged with Ringer's lactate, and it is interesting to note the nonprotein nitrogen in the gastric washings was 50 mg. per cent one day, and 27 mg. per cent the next. Recovery was complete a month postoperative.

Originally this case was listed under the heading of "dehydration," but the anuria from dehydration alone should be relieved promptly by remedying the dehydration. The duration and other features of this case indicate that there must have been cell damage, and it should properly be listed as a case of lower nephron nephrosis.

Case 16. A 50 year old man with an initial blood pressure of 200/112 had an abdominoperineal resection for adenocarcinoma of the rectum. During the operation the blood pressure dropped markedly, and he received 1500 cc of whole blood. Immediately after operation, the systolic pressure fell to 70 and clinical signs of shock were evident. An additional 1000 cc blood and 1000 cc 50 per cent glucose were given in the first 24 hours, when his blood pressure stabilized at 120/80. In the first 24 hours, the urinary output was 30 cc, the next day 250 cc, and 600 cc on the third day. By the fifth day the nonprotein nitrogen was 221 and the chlorides had dropped to 221. Fluids were limited to 2000 cc daily. He died on the sixth day and autopsy showed changes in the distal tubules characteristic of the lower nephron syndrome.

Treatment here can be criticized; after initially replacing blood fluid loss in order to bring the blood pressure up to reasonable levels, the fluid intake should have been reduced to maintenance levels. There was no pulmonary edema in this case, however, and probably the excess fluid played no part in the outcome. The failure to establish electrolyte equilibrium may have played some part.

Case 17. A 68 year old woman had been given 4 gm. sulfadiazine for acute cystitis 3 days before admission. Apparently there was almost immediate anuria in spite of the fact that she drank plenty of fluids. She became drowsy and stuporous and was admitted semicomatose with a nonprotein nitrogen of 100, and a CO_2 of 28.7. Cystoscopy showed 250 cc in the bladder; the ureters were easily catheterized and urine was obtained from each pelvis. No crystals were seen. The first day, 200 cc drained from the ureteral catheter; the following day 1255 cc, and on the fourth day 3200 cc were obtained. Pyelograms then showed slight hydronephrosis on each side. The catheters were removed and she voided spontaneously and adequately thereafter. The nonprotein nitrogen reached a peak of 118 on the fourth hospital day, and reached normal on the thirteenth. She has remained well. In this case, one complicating factor was a history of carcinoma of the cervix treated by panhysterectomy 7 years before. There was no sign of recurrence at the time of this episode.

Case 18. A 42 year old man had been treated for pneumonia by 60 gm. of sulfapyridine. He became unable to void, and his physician was unable to pass a catheter. In the emergency room, filiforms were tried and a No. 18 follower catheter passed producing no urine. A false passage was feared. The patient was very heavy and the bladder seemed distended so a trocar was tried without result and a suprapubic cystotomy was done, no urine being found in the bladder. The bladder was closed tightly and an indwelling catheter strapped in place. The nonprotein nitrogen on admission was 77. He began secreting urine the night after operation, and his output gradually returned to normal and the nonprotein nitrogen fell gradually to normal. The suprapubic wound healed per primam and he was discharged well, at the end of 12 days, and has remained well. His renal function is normal so far as can be determined. We are not particularly proud of our record here.

Case 19. A woman of 23 years was delivered, by forceps, of a frank breech presentation. Anuria developed immediately after delivery, and the nonprotein nitrogen rose to 130 mg. in 8 days. Cystoscopy showed marked edema of the trigone; only the right ureter could be catheterized, and no urine drained from it. She was treated by limiting fluids to 2000 to 2500 cc daily, and renal diathermy. Her face and body became very puffy, but there was no pulmonary edema. Urine appeared in 7 days and her nonprotein nitrogen continued to rise for 4 days, and then began to drop, and became normal 10 days later. Two days after anuria ceased she began to have profuse diuresis. She was put on full diet and no effort was made to give chlorides in any other form. Recovery was complete as evidenced by normal urea clearance, normal nonprotein nitrogen and normal intravenous pyelograms.

The treatment here is open to criticism. Fluids were not forced, it is true, but they were not adequately limited. Apparently regeneration occurred sufficiently early to take care of a moderate excess of fluid before the circulation became embarrassed.

Case 20. A 26 year old woman in the sixth month of pregnancy had a mild toxemia, and was delivered of a still-born baby. Following this, she passed no urine. On admission, her blood pressure was 160/100 and cystoscopy showed no urine in the bladder, no ureteral obstruction and no urine in the renal pelves. The nonprotein nitrogen rose to 90 on the third day adter admission; when 75 cc of urine were obtained by catheter, on the fourth day, 175 cc; and on the fifth, 275 cc; on the sixth, 150 cc. On the seventh day, 375 cc were obtained, and from this day on, the output steadily improved, although the nonprotein nitrogen continued to rise until it reached 158 on the eleventh day after admission, and did not reach normal until the nineteenth day after admission. She was in apparently good condition all the time, and the only treatment she received was the limitation of fluids to 1500 to 2000 cc daily in the early days until the urinary output began to increase. No attention was paid to the CO_2 combining power, nor to the electrolytes. (See figure 2. In this chart, the peaks on the intake curve indicate compensation for vomiting.)

Case 21. A 27 year old woman had a transfusion reaction followed 3 days later by nausea, vomiting and epigastric pain. Acute pancreatitis was suspected, and the diastase was found to be 70. The urinary output diminished, and no urine was obtained on the ninth day after the transfusion, and her nonprotein nitrogen was 142. The diastase dropped to 58, and the urinary output gradually increased and the nonprotein nitrogen and diastase decreased until normal levels were reached on the twenty-eighth day after the transfusion. The diagnosis was transfusion reaction with acute pancreatitis, and lower nephron nephrosis. She has been well since. She had a stomach tube with continuous suction, and received between 2000 and 2500 cc fluid by vein and tube each day, probably a slight excess over the ideal.

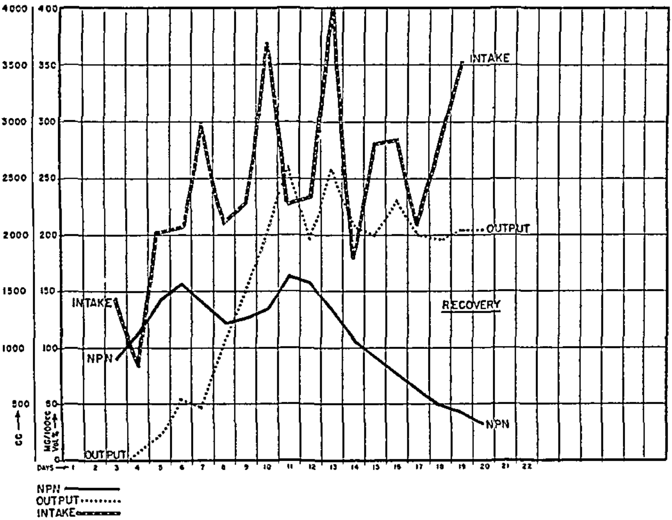


FIG. 2. Anuria-Post Partem-Toxemia of Pregnancy #529097

Case 22. A 52 year old man, following transurethral resection, began to have fever and was given sulfathiazole, 1 gm. every 6 hours. He became toxic, developed anuria, and had a rash over his whole body. He became jaundiced, and died in what was thought to be uremic coma, with a nonprotein nitrogen of 96 on the eighth day postoperative. He was treated by forcing fluids. This occurred in 1943, and by hindsight, we can see that this was a case of so-called intravascular hemolysis, and that our treatment was very bad. Unfortunately, there was no autopsy, but we can feel sure that the characteristic lesions of lower nephron nephrosis would have been found.

Case 23. A man 50 years old, at the time of an abdominoperineal operation for rectal carcinoma, received 200 cc pectin and 1000 cc blood, followed by severe reaction, and anuria, becoming oliguria. He died 6 days later. The nonprotein nitrogen rose to 118 three days before death. The carbon-dioxide combining power was 33.4 at one time. The treatment was forcing fluid between 3000 cc and 6000 cc daily. Death was accompanied by pulmonary edema. Autopsy showed the typical lesions of lower nephron nephrosis. His chances of survival would have been better if treatment had been less vigorous.

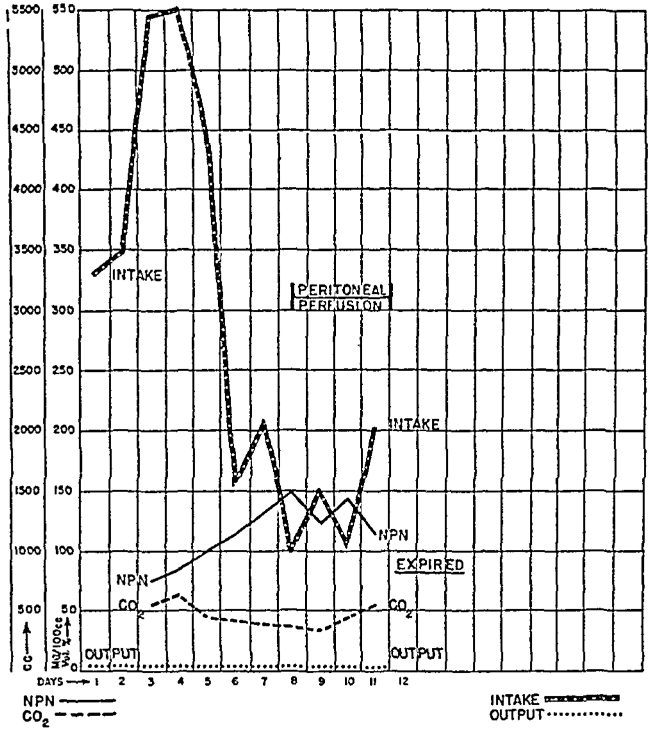


FIG. 3. Sulfadiazine Anuria #391374

Case 24. A 35 year old man received 60 gm. of sulfadiazine in 2 doses for a respiratory infection. He noted nausea and vomiting and the next day passed no urine. A small amount of urine examined, showed blood cells, but no crystals. He was then admitted to the hospital. Cystoscopy showed 5 cc fluid in the bladder, no ureteral obstruction, and no urine in the pelves. Fluids were forced to 5000 cc. The nonprotein nitrogen rose gradually, his face became edematous. Five days after admission, the nonprotein nitrogen was 127, and there was evidence of pulmonary edema. Peritoneal lavage was instituted, and the patient put in oxygen. He was perfused with Ringer's lactate with 10,000 units of penicillin added to each litre of solution. During the next 12 hours, due to technical difficulties only 240 cc of fluids perfused. Followed this, satisfactory drainage was established, and perfusion maintained at an average of 12,000 cc daily. On one day, 10 per cent glucose solution was used in the hope of withdrawing some fluid from the lungs, with some clinical evidence of improvement. After this, Ringers lactate solution was used. Perfusion was used for 4 days until the patient rather suddenly expired, 9 days after admission. Autopsy showed marked pulmonary edema, and the kidneys showed the characteristic lesions of lower nephron nephrosis.

This case merits some discussion. The early treatment was wrong. There was no necessity of replacing a large amount of fluid, or in raising his blood pressure, so the initial intake of 5000 cc was an error. Also, for a few days, he received 3,000 cc per day, and this being considerably more than his output, accumulated in his body, of which evidence was given by facial edema, and pulmonary moisture. The following tabulation and the diagram (fig. 3) show some interesting features in the course of the patient. It will be noted that the nonprotein nitrogen could be lowered by perfusion, and that the perfusion fluid showed a nitrogen content. The chloride and carbon dioxide determinations showed no marked change throughout.

DATE	BLOOD			PERFUSION FLUID
	NPN	CO_2	Cl	NPN
Adm.				
4/8	38			
4/10	74	52.2		
4/12	106	48.3	467	
4/14	127	51.3		
Perfusion Instituted				
4/15	150 A.M.		413	64.5
	146 P.M.			131
4/16	125	35.9	453	
4/17	145	44.4	473	125
4/18	119	52.8	460	91.2

Case 25. A 64 year old man had shown himself sensitive to sulfathiazole. He was thought to have pneumonia, and was being treated with sulfadiazine, which he tolerated well. By mistake he was given two tablets of sulfathiazole, and immediately reacted amazingly. His temperature went to 103 F., and he ceased to urinate. The anuria persisted for 7 days "despite liberal administration of intravenous fluids," caffeine, and renal diathermy. The nonprotein nitrogen rose as high as 108. On the eighth day, the urinary output began to increase and slowly returned to normal. He was eventually discharged after 30 days in the hospital, at which time the nonprotein nitrogen was 40 and the phenolsulphonphthalein 17 per cent in 2 hours. Later, the phenolsulphonphthalein increased to 66 per cent in 2 hours. The patient recovered in spite of our efforts.

Case 26. A man of 52 years was admitted to the hospital 2 days after becoming ill with acute hepatitis. Treatment consisted of intravenous 10 per cent glucose. The urinary output diminished to nothing the fourth day of hospitalization, and the anuria persisted until his death on the sixth hospital day. On the fourth day, the nonprotein nitrogen was 108 and the artificial kidney was connected to the femoral vein by a catheter. His fluid intake was over 3,000 cc per day, and death was accompanied by pulmonary edema. The artificial kidney did not improve his clinical condition. Unfortunately, no autopsy was permitted.

Case 27. A man of 65 years had been given 4 gm. of sulfadiazine daily for 4 days, in treatment of an eye infection. He had chills and fever, the urinary output diminished, and for 2 days before admission he had voided no urine at all.

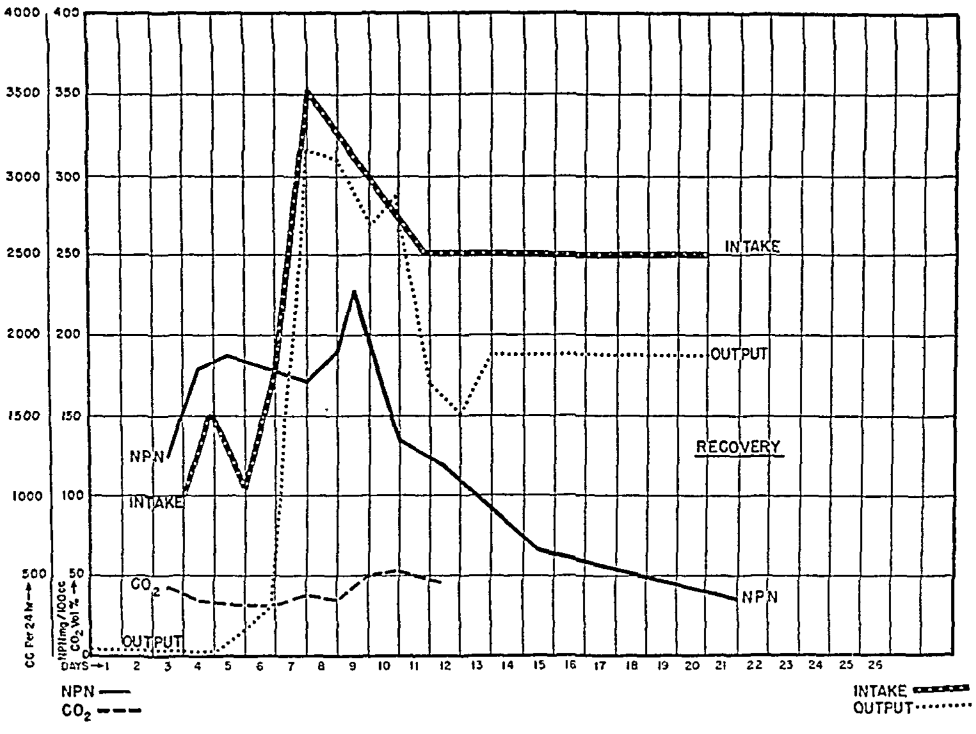


FIG. 4. Sulfadiazine Anuria #367368

Cystoscopic examination showed no urine in the bladder and catheters were easily passed to the pelvis; 5 cc of urine was obtained from the right pelvis, and this contained no sulfa crystals. He was placed on a limited fluid intake, attempting to replace only the amount lost by respiration and perspiration. The nonprotein nitrogen on admission was 125, and the next day it was 180; the following day, 185. On the second day of hospitalization, a two way Miller-Abbott tube was introduced, and gastric and duodenal lavage instituted. The amount removed was subtracted from the amount given, and enough fluid given intravenously to keep the daily intake between 1200 and 1500 cc. The chlorides and the carbon-dioxide combining power remained within reasonable limits. On the fourth day of admission, 6 days after the onset of anuria, he voided 340 cc urine, and the amount steadily increased each day. The lavage was discontinued and fluids were forced by mouth. The nonprotein nitrogen continued to rise for 2 days after the onset of diuresis, rising to 229, and then gradually declining to normal 25 days after the onset of his illness. During the period of diuresis, except for the administration of a normal diet, no effort was made to give chlorides, and there was no evidence of excessive output of chlorides.

It is interesting that clinically this man never seemed to be in critical condition. He remained reasonably alert all through. Figure 4 is self-explanatory.

DISCUSSION

We have here reported 27 cases of anuria of various kinds, some recent, some occurring several years ago. In some, the urological division was completely responsible for the care; in some, it shared in the responsibility; and in some, it played no part. What we can now see to have been errors in treatment, we have endeavored to bring out.

The most interesting group is that of the lower nephron nephrosis, in which group we have included 13 of our patients. Of these 13 patients, 5 died. By hindsight, we can say that in all these 5 cases, the treatment was faulty. This is not to say that all would have recovered, if the treatment had been different. Three of them would certainly have had a better chance to recover, had they received more rational treatment. The other 2 patients had been subjected to exceedingly extensive and shocking operations, and undoubtedly hemorrhage played a large role; it is probable that no treatment would have offered much hope. It is suggestive that pulmonary edema was present in four of the cases.

It is also interesting and suggestive that all of our patients who received treatment that we would now consider reasonably satisfactory, recovered.

Of the 8 of our patients who recovered, 2 may be said to have received excellent treatment; 4, to have received satisfactory treatment; and 2 recovered in spite of the treatment given.

It has been shown by various authors, that when diuresis begins, there may be a drain on the chlorides, and it may be necessary at this time, to give chlorides as well as increased fluids. This did not occur in any of our patients. In no case was it necessary to give more chlorides than they received in the diet.

In addition to the regimen described above certain other methods have been suggested, and used, in the hope of re-establishing renal function in these cases; decapsulation, spinal anesthesia and parasympathetic block.

We have tried decapsulation, with no success; but not in cases of the lower nephron syndrome. As Thorn stated, it seems probable that when it has seemed successful, it has been done at the moment when diuresis was about to commence.

We have had no experience with spinal anesthesia or parasympathetic block. They seem rational procedures on the basis of Trueta's theory of neurogenic cortical ischemia and anoxia, particularly if done early, before extensive necrosis of the tubule cells has taken place. There are reports in the literature of favorable effects of these measures.

Renal diathermy is another measure that has a rational basis. We have used it, but cannot tell whether it has helped or not. It is completely harmless, however, and we felt it worth trying.

There are four methods designed to reduce the amount of waste products of metabolism in the blood: sweating; the artificial kidney; peritoneal perfusion; and gastric lavage. We have used sweat baths in the past, with what results we are not prepared to say. The artificial kidney was tried on 2 of the patients reported here. In 1 case, it was not possible to connect it correctly, so it was useless, though it did no harm; in the other, it may have contributed to the fatal outcome because of hemorrhage and clotting.

Peritoneal lavage was tried in two instances. In both cases, it seemed to function well. Substantial amounts of nitrogen were found in the perfused fluid and the nonprotein nitrogen of the blood simultaneously either stabilized or diminished. It is simple to install. Our method was to introduce a Pezzer catheter into the peritoneal cavity, high in the right flank for intake, and sump drain in the lower left quadrant, connected with suction, for outlet. The chief drawback was that it required the full-time attention of someone, nurse or physician, to toy with the outlet to keep the fluid running. The omentum has a tendency to wind itself about the outer tube of the drain. It was rather interesting to see how, by altering the constitution of the perfusing fluid, alterations in the blood chemistry could be brought about.

Both patients on whom we used this method died, and autopsy showed no peritonitis, but did show opacity and thickening of the peritoneum, suggesting that the period of effectiveness of such a perfusion would be limited.

Finally, we must consider gastric and duodenal lavage. In the few cases in which this was used, we were very favorably impressed. We were able to stabilize or diminish the nonprotein nitrogen of the blood, and we could add or extract fluid or salt. It is a harmless and easy procedure, and the patients do not object to it. Our experience leads us to prefer it to the other methods mentioned.

As we sum up our experience then, we believe the following conclusions are justified:

There is no demarcation between oliguria and anuria.

Cystoscopic examination is indicated in the majority of cases, to distinguish between the obstructive and secretory types.

The obstructive type is easily remediable, if the obstruction can be removed.

In the treatment of the secretory type, it is most important not to force fluids after the initial restoration of blood volume and blood pressure. Replacement of fluid and electrolyte loss, plus a high caloric, low protein diet are indicated.

In long continued cases, some means of removing waste products from the blood are probably useful. In our experience, gastric and duodenal lavage is satisfactory and simple.

Most patients with uncomplicated lower nephron nephrosis will recover, if not drowned.

REFERENCES

ABESHOUSE, B. S. AND TANKIN, L. H.: Renal complications of sulfonamide therapy. J. Urol., **56**: 652–657, 1946.

BURWELL, E. L., KINNEY, I. D. AND FINCH, C. A.: Renal damages following intravenous hemolysis. New Eng. J. Med., **237**: 657–665, 1947.

Corcoran, A. C. and Page, I. H.: Crush syndrome: Post-traumatic anuria. J. A. M. A., 134: 436–441, 1947.
Creevy, C. D.: Hemolysis during transurethral resection. J. Urol., 58: 129–131, 1947.
Fine, J., Frank, H. A., and Seligman, G. M.: The treatment of acute renal failure by peritoneal irrigation. Ann. Surg., 124: 857–878, 1946.
Lattimer, J. K.: A plan for management of anuria. J. Urol., 54: 312–317, 1945.
Lucké, B.: Lower nephron nephrosis. Mil. Surg., 99: 371–396, 1946.
Thorn, G. W.: Treatment of renal insufficiency. J. Urol., 59: 119–148, 1948.
Trueta, J., Barclay, A. E., Daniel, P. M., Franklin, K. J. and Pritchard, M. M. L.: Studi [illegible] arles C. Thomas, 1947.
Van Slyk [illegible] nt. Med., 28: 701–722, 1948.
Vermooten, V. and Hare, D.: Gastric lavage in the treatment of uremia. J. Urol., 59: 907–919, 1948.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

DISCUSSION

DR. EVERETT E. ANGLE (Lincoln, Nebr.): It is a pleasure to open the discussion of Dr. Ormond's courageous paper on this broad subject of anuria. The treatment of anuria is a problem worthy of our best efforts, both collectively and individually.

I agree with his classification and know that ureteral catheterization in a case where there is obstruction of ureteropelvic juncture and in every case where there is the slightest possibility of finding an obstruction and relieving such obstruction, is one justification of our specialty.

Let me quickly summarize a case that shows a little different problem in this group. A boy of 3 years was brought into the hospital with a history of having had his appendix removed, and on the eleventh day started to have trouble with distention and toxic symptoms. There was a question as to whether he had an obstructive lesion or not, because he had had complete anuria for 2 days and no one knew how much urine he had passed for several days before that.

I saw him two days later, or on the fifth day after anuria, and attempted to catheterize the ureter and failed to find either orifice. The bladder was too congested. The next morning we explored his left renal area because there was a slight, vague shadow in the x-ray, and nothing on the right. I found a distended kidney. A nephrostomy tube recovered 300 cc urine, and he got along fine. A month later a plastic operation was done to relieve two bands causing the kink.

The treatment of the second, or secretory, type of anuria is an entirely different matter and intrigues one to use medical rather than surgical skill. There is an optimum amount of fluid to give any case of renal insufficiency, and to give more than this amount is bad in every case, but the lower the renal function, the greater the danger in too much intravenous fluid.

I agree that sweating is probably useless and possibly harmful. I know nothing of artificial kidney or peritoneal lavage, but think the Scientific Exhibits here are most interesting.

I hope you are not all going to refuse to do renal decapsulation. It can be done so quickly that there is little to lose, and it preceded recovery in 2 cases recently in Lincoln: One, a man, 43 years old, was under treatment for hepatitis following cholecystectomy. He was given 2.5 gm. sodium sulfathiazole intravenously. Anuria developed immediately. He was really shut off, and on the evening of the third day the blood urea was 187. The CO_2 combining power was 56 per cent, about normal, but the attending physician wished to have the kidneys explored, and we did a decapsulation, which took 40 minutes from beginning to end. Although the patient passed very little urine the first day, in the next 16 hours he put out 400 cc and went on to complete recovery.

Decapsulation is not without merit.

In closing, let me suggest this subject to the Program Committee for a symposium rather than a paper.

DR. ABRAHAM D. SEGAL (Brooklyn, N. Y.): I wish to compliment the authors on their timely paper I should like to discuss one type of anuria In 1936 Dr J Sturdevant Reid and myself brought out the syndrome of acute anuria in perforated gastric lesions, whether malignant or ulcer, and which do not present the usual crisis of the acute abdomen The syndrome has been misinterpreted for acute retention but it is really anuria on a dehydration basis

These people give a history of having taken bicarbonate and having other gastric disturbances The fluid intake passes into the peritoneal cavity which, with the suceeding inflammatory reaction, loses its absorptive powers, and a state of dessication and electrolyte imbalance ensues

Due to the encapsulation of the intraperitoneal fluid, one receives the impression of a doughy suprapubic mass Likewise the pressure of the aggregation of fluid causes a sensation of frequency, but without relief, and no emission of urine Insertion of a catheter reveals an empty bladder

Rectal examination in most of the cases yielded a small prostate in its normal position, in contradistinction to the large prostate, which protrudes so often into the rectum as a result of the full bladder

This anuria is prerenal in origin and it should be recognized as an entity which requires immediate surgery, antibiotics, fluids, and the establishment of an electrolyte balance

Dr John K Ormond (Detroit, Mich) There are three slides I should like to show

(Slide) This first one shows how a case should not be treated A man with anuria was given 5000 cc fluid the first day, then for a couple of days he received around 2000 At this point, peritoneal perfusion was started and here is the nonprotein nitrogen There seems to have been some effect on it He died. We had an autopsy and he had very marked pulmonary edema We knew that he had that all the time

(Slide) This is a case that I think shows how a patient should be treated This was another sulfonamide anuria You will note the urinary output When it started to rise, we pushed up the fluids and you can see how the fluid intake and the output were parallel after that

An interesting point about these cases is that the nonprotein nitrogen will continue to rise for 2 or 3 days after diuresis starts Then it starts to fall In this case the CO_2 never changed It was not necessary in this case to give chlorides, because the chlorides stayed at this level with just the ordinary diet

(Slide) This is another patient with recovery She had toxemia of pregnancy

I wish to thank Dr Angle for his discussion, and say that I have not seen any such cases as Dr Segal reported

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

MANIFESTATIONS OF THE LYMPHOBLASTOMAS IN THE GENITO-URINARY TRACT[1]

ERNEST M. WATSON, HANS R. SAUER AND MARVIN G. SADUGOR

From the Roswell Park Memorial Institute, Buffalo, N. Y., and the Department of Urology, School of Medicine, University of Buffalo, Buffalo, N. Y.

Study of the literature indicates that recognition of lymphoblastomatous involvement of the urologic tract often represents diagnostic difficulties and a substantial number of publications are on record where the true nature of the disease was recognized only after employment of ill-advised surgical procedures (Kretschmer, Pease and McDonald, Mathé, Jacobi, Panoff and Herzlich, Marshall and Shnittman, McCrea, Flaherty, Cope and Shecket, etc.). For the most part, the literature on this subject is comprised of case reports in which lymphoblastomatous involvement of various organs of the genito-urinary tract has been described. More detailed studies of this problem have been presented by Barney, Hunter and Mintz (1923), and more recently by Meyer (1941), Merrill and Jackson, Jr. (1943), as well as Kirshbaum and Preuss (1943). Barney, who based his report on a review of 51 autopsies of patients with lymphoblastomas, determined urinary tract involvement in 33 or 64.7 per cent of the cases. An incidence of 68.3 per cent was reported by Kirshbaum and Preuss, who based their studies on postmortem examination of 123 patients with leukemia.

Although these reports suggest that lymphoblastomatous involvement of the genito-urinary tract is a common finding on postmortem examination, it must be remembered that the clinical manifestations produced by these changes are comparatively infrequent. This paucity of urological symptoms in patients with lymphosarcoma, leukemia or Hodgkin's disease accounts for the fact that the urologist is only rarely called upon to examine these cases. Nevertheless, complications requiring intervention by the urologist may arise in any patient with lymphoblastoma, and, in some instances, the urologist may even be consulted first because the initial manifestations of the disease suggest primary urologic tract disease. Particularly in the latter group of cases, where the clinical picture is dominated by the prominence of the urologic symptoms, the true nature of the underlying condition may easily escape early recognition. Therefore, in order to avoid errors, which may have far-reaching consequences, it is of prime importance to be conscious of the possibility that certain lesions encountered may represent manifestations of lymphoblastoma and not primary disease of the genito-urinary tract.

While the correct interpretation of urological complications may represent no difficulties in patients who are known to suffer from lymphoblastoma, it is not easy in undiagnosed cases to recognize such a lesion on first examination, inasmuch as the clinical manifestations produced are in no way characteristic.

Uremia, hematuria, obstructive symptoms, frequency and dysuria, or tumefaction of the testicles may be the initial symptoms of the disease and prolonged clinical and laboratory investigations are often required before the true character of the condition is recognized.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 19, 1948.

The following presentation has been occasioned by the observation of several patients who were referred to the urological service of the Roswell Park Memorial Institute because of primary manifestations of lymphoblastoma in the genito-urinary tract. The diagnostic difficulties encountered in these cases have stimulated interest and prompted a more detailed study of this subject. To this end, a review of 1073 cases of lymphoblastomas admitted to this institution during a 35 year period, was undertaken and data with regard to the incidence of urologic tract involvement were collected. Four hundred and fifty-six of these patients had lymphosarcoma, 234 had leukemia and the remaining 383 had Hodgkin's disease.

TABLE 1 *Involvement of urologic tract by lymphoblastomas*

	OVER ALL INVOLVEMENT OBSERVED IN 1073 CASES			INVOLVEMENT OBSERVED IN 143 AUTOPSIES		
	No of cases	Involvement determined	%	No of cases	Involvement determined	%
Lymphosarcoma	456	43	9.5	52	32	61.9
Leukemia	234	32	13.5	46	27	58.6
Hodgkin's disease	383	5	1.3	45	3	6.6
	1073	80	7.5	143	62	43.4

Various degrees of involvement of the urologic organs were determined in 80 or 7.5 per cent of the 1073 cases. The incidence of these manifestations was highest in patients with leukemia (32 or 13.6 per cent of 234 cases) and lymphosarcoma (43 or 9.5 per cent of 456 cases) and comparatively infrequent in patients with Hodgkin's disease (5 or 1.3 per cent of 383 cases).

However, it must be understood that these figures do not give a true picture of the actual occurrence of such lesions, since there existed a very marked discrepancy between the incidence of urologic tract involvement as determined by clinical findings and by postmortem examination. It was found that urological manifestations of the disease were demonstrable in 62 or 43.3 per cent of 143 autopsy cases. Also, in this material, it was determined that the patients with leukemia (27 or 58.6 per cent of 46 cases) and lymphosarcoma (32 or 61.9 per cent of 52 cases) showed a much more common occurrence of urologic tract involvement than those with Hodgkin's disease (3 or 6.6 per cent of 45 cases). (See table 1.)

Several reasons can be advanced why autopsy studies only can supply accurate data as to the actual incidence and extent of the pathological changes produced by lymphoblastomatous involvement of the urologic organs. For instance, the absence of urological symptoms does not necessarily preclude urologic tract involvement, because the lesions may be either too small to cause symptoms or under certain conditions they may remain asymptomatic in spite of being extensive. This is substantiated by the observation that clinical, as well as laboratory findings are often negative for urological tract involvement, even during the terminal stages of the disease although subsequent postmortem examination may reveal considerable urinary tract disease. In addition, it must be understood also, that urological symptoms, particularly in patients with advanced disease, are prone to be overshadowed by the severity and acuteness of other more prominent manifestations of the disease.

It ensues from the above discussion that it is quite possible that urologic tract involvement may escape the attention of both the patient and the physician. This is borne out by the fact that 57 or 71.3 per cent of the 80 patients who fell into this category had no record of urological symptoms throughout the course of the disease (table 2). Of the urological manifestations produced by lymphoblastomatous involvement in the remaining 23 patients, bleeding was the most common symptom (7 patients). It was determined, furthermore, that symptoms referable to the genito-urinary tract represented the first manifestations of the disease in 5 of the latter group of 23 cases. The initial symptoms in these 5 patients were as follows:

TABLE 2. *Urological symptoms produced by lymphoblastomatous involvement of the genito-urinary tract in 80 cases*

Asymptomatic throughout	57
Hematuria	6
Bleeding from local lesions	1
Pain in kidney region	2
Uremia	3
Urinary retention	2
Frequency and dysuria	1
Incontinence of urine	1
Edema of penis and scrotum	4
Priapism	1
Tumefaction of testicles	2
Total	80

	Cases	
Painless hematuria	2	(lymphosarcoma of kidneys)
Bleeding from local lesion	1	(lymphosarcoma of female urethra)
Urinary retention	1	(lymphosarcoma of prostate)
Tumefaction both testicles	1	(leukemia of testicles)

Of our 80 cases, an analysis with regard to the organs involved revealed as an outstanding fact that the kidneys were predominantly affected (66 patients or 82.5 per cent), but lymphoblastomatous involvement was also observed in the kidney pelves, ureters, bladder, prostate, testicles, penis and urethra (table 3). While the lesions remained confined to one urologic organ in 55 patients, involvement of more than one was demonstrable in 13 patients; in the remaining

8 cases, the exact number of genito-urinary organs involved could not be determined because no autopsy was obtained.

TABLE 3 *Urologic organs involved by lymphoblastomas in 80 cases*

	LYMPHOSARCOMA 43	LEUKEMIA 32	HODGKIN'S DISEASE 5	TOTAL 80
Kidneys	34	30	2	66
Kidney pelves	9	2	1	12
Ureters	9	4	1	14
Bladder	5			5
Prostate	3			3
Penis		2	2	4
Testicles	2	1		3
Urethra	1			1

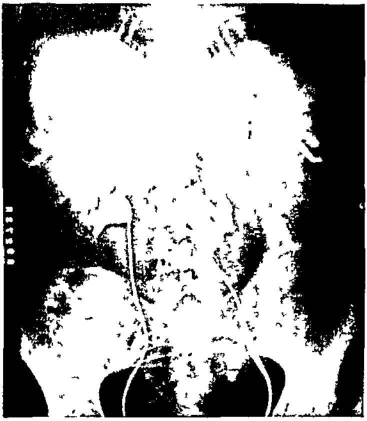


FIG 1 Downward and medial displacement of left kidney and ureter by splenomegaly

KIDNEY

Many variations of clinical and pathological changes occurring singly or in combination, may be produced in the kidneys as a result of involvement from lymphoblastoma.

1) Displacement of the kidneys in any direction may take place as a result of splenomegaly or formation of retroperitoneal lymphoblastomatous tumor masses (fig. 1). The frequency of its occurrence cannot be determined with any degree of accuracy, since this condition rarely produces urological symptoms and for this reason no urological investigation is requested, as a rule. In addition, it must be remembered that negative findings at the time of examination need not necessarily preclude the possibility of previous kidney displacement

since return to its original position is the rule if regression of the displacing tumor masses occurs following initial treatment of the primary disease. If investigated, the diagnosis of this condition offers no difficulties: displacement of the kidney can be determined in certain cases, by palpation, but pyelographic studies are necessary in order to obtain more accurate information.

2) Invasion of one or both kidneys by direct extension from perirenal tumor masses may be encountered on postmortem examination in patients with extensive retroperitoneal lymph node involvement. Yet, although the kidneys were quite commonly found imbedded in lymphoblastomatous tumor growth, direct infiltration of the kidney through its capsule was noted in only 5 cases (fig. 2).

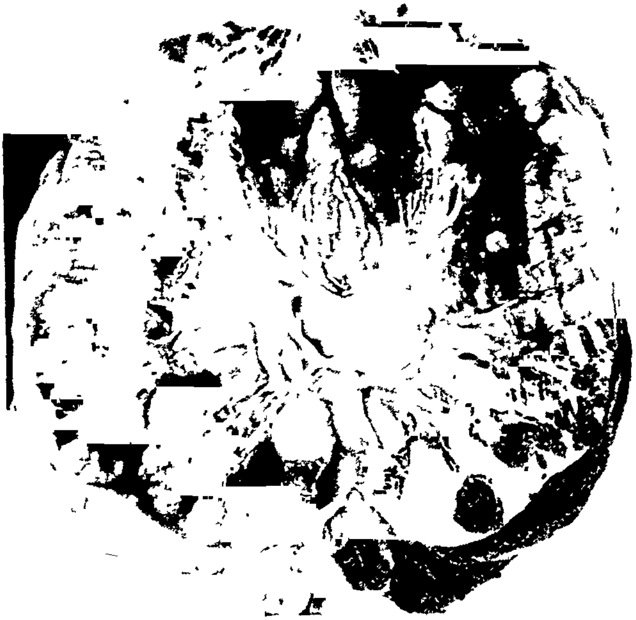


Fig. 2. Extensive lymphcsarcomatous involvement of kidney

3) Macroscopic involvement of the renal parenchyma in the form of multiple nodules of varying size is the most frequently encountered picture (fig. 2). Occasionally, a single lesion may constitute the only evidence of renal involvement, but also infarction is encountered in isolated cases.

The symptoms produced by these changes are primarily determined by the type of lesion present. For example, if infarction occurs, profuse hematuria may result (fig. 3); in contrast, symptoms may be absent or insignificant in patients with solitary or multiple foci. In the latter group of cases slight albuminuria, microscopic hematuria with or without casts, may be the only findings; however, it has been noted that the urinary findings were sometimes minimal, in spite of extensive kidney involvement. Depending on the degree of parenchymal destruction, impairment of kidney function takes place and in certain cases, where large areas of the kidney parenchyma have been replaced by tumor growth, oliguria followed by uremic symptoms may occur. Early recognition of such a condition is of prime importance in these cases, because prompt initiation of appropriate treatment will, at least temporarily, not only arrest but also induce regression of the basic underlying disease.

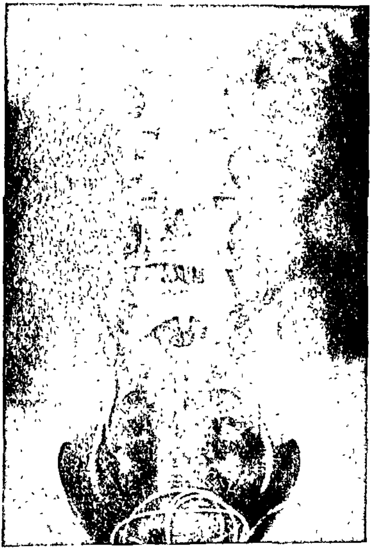


Fig. 3. Hematuria from right kidney causing filling defects in right ureter due to blood clot formation. Autopsy 2 weeks later revealed large infarct in right kidney and normal ureter.

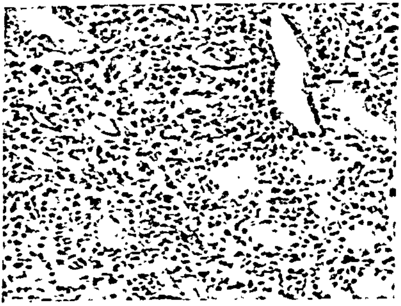


Fig. 4. Lymphoblastomatous infiltration of intertubular spaces of kidney

4) *In kidneys which apparently are unaffected on gross inspection,* various types of microscopic lesions may be demonstrable singly or in combination in either all or some parts of the renal parenchyma (fig. 4). These findings may

consist of a) diffuse infiltration of the intertubular spaces, b) involvement of the periglomerular structures, or c) invasion of the perivascular spaces. As these changes progress, compression of the secretory units frequently associated with stasis in the smaller blood vessels takes place often resulting in gross hematuria, but, also uremia may develop during the more advanced stages of the disease. It ensues that the possibility of this pathological picture should be entertained in patients with urologic tract symptoms where pyelographic studies fail to show morphological abnormalities.

TABLE 4. *Pathological changes produced in 80 patients with urologic tract involvement from lymphoblastoma*

		LYMPHOSARCOMA 43 PATIENTS	LEUKEMIA 32 PATIENTS	HODGKIN'S DISEASE 5 PATIENTS	TOTAL 80 PATIENTS
Kidney	Displacement	2			2
	Invasion from without	4	1		5
	Multiple or single macroscopic nodules	17	10	2	29
	Infarction	1			1
	Microscopic involvement	7	18		25
	Clinical evidence (functionless kidney, uremia)	8	3		11
Kidney pelves	Direct invasion	1			1
	Dilatation	8	2	1	11
Ureters	Displacement	5	2		7
	Direct invasion	1			1
	Dilatation	7	2	1	10
Bladder		5			5
Prostate		3			3
Penis			2	2	4
Urethra		1			1
Testicles		2	1		3

It may be difficult at times to establish a clinical diagnosis of kidney involvement by lymphoblastoma. The urinary findings are usually not characteristic but rather suggest chronic nephritis which is known to occur during the terminal stages of any malignant disease. Even in patients where gross hematuria, loss or impairment of kidney function, obstructive symptoms or pyelographic changes give evidence of renal involvement by lymphoblastoma, it is almost impossible to conclude with what types of pathological changes one is confronted in each individual case. Furthermore, it must be remembered that the urologic tract lesions as demonstrated on one occasion need not remain constant but are apt to undergo partial or complete regression following therapy. This latter fact accounts for the discrepancy between the clinical and the postmortem findings which are encountered at times.

Study of the data collected indicated that renal involvement predominated in the group of 32 leukemia patients where kidney lesions were determined in 30 or 93.8 per cent of the cases. This compares with an incidence of only 34 or 79.1 per cent in 43 patients with lymphosarcoma. The number of patients with kidney involvement from Hodgkin's disease is too small in this case series to permit conclusions.

A further analysis of this material disclosed interesting observations with regard to the type of renal lesions encountered in the group of patients with leukemia and lymphosarcoma; namely, it was noted that microscopic infiltration of the kidney parenchyma was much more common in patients with leukemia (18 or 60 per cent of 30 cases) than in patients with lymphosarcoma (7 or 20.6 per cent of 34 cases) (table 4). Significantly enough, it was also observed that macroscopic kidney lesions from leukemia were usually less numerous and less extensive than those from lymphosarcoma which indicates that lymphosarcoma shows a higher degree of invasiveness.

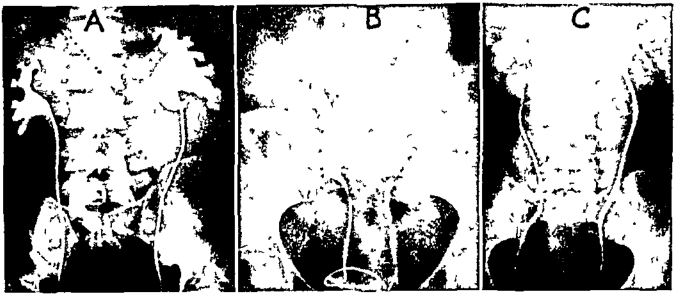


FIG. 5 *A*, hydronephrosis, left kidney and lateral displacement of ureter due to retroperitoneal lymphoblastomatous tumor masses. *B*, medial displacement and obstruction of both ureters by lymphosarcomatous tumor growth encompassing pelvic brim *C*, bilateral lateral displacement of ureters by extensive retroperitoneal lymphosarcoma.

KIDNEY PELVES AND URETERS

Dilatation and/or displacement of kidney pelves and ureters due to adjacent tumor masses is common in patients with lymphoblastomas (fig. 5, *A*), yet direct invasion of these organs may also be found occasionally. The type and the extent of these changes depend largely on the location of the tumefaction; for instance, it was noted that dilatation of kidney pelves and ureters occurred predominantly in patients with lesions encompassing the pelvic brim (fig. 5, *B*) (Marshall and Schnittman), while involvement of the lymphatics surrounding the more proximal parts of the upper urologic tract was more apt to cause displacement (fig. 5, *C*).

In rare instances, hydronephrosis may be produced by leukemic marrow which forms around the hilus of the kidney. This condition, which has been described by various authors (Moore, Meyer, Parkes-Weber, a.o.) has not been observed in this case series.

The symptoms most commonly produced by the aforementioned lesions consist of varying degrees of obstructive manifestations. In addition, gross hematuria may occur as a result of direct invasion of kidney pelvis and ureter or due to secondary changes in the renal parenchyma. Other patients, however, will remain asymptomatic.

Urological examination is of significant diagnostic value in these cases since pyelograms may demonstrate the presence of retroperitoneal masses in some patients where palpation is not conclusive. Furthermore, by comparative study of subsequent urograms, the effect of therapy directed against these lesions can be evaluated more accurately.

FIG. 6. Circumscribed solitary lymphosarcomatous tumor nodes in outer bladder wall

BLADDER

Involvement of the bladder by lymphoblastoma is extremely rare. This is borne out by the paucity of the literature on this subject which consists either of isolated case reports (Kirshbaum and Preuss, Pentecost and Pizzolato, a.o.) or of casual references to its occurrence (Huggins and Johnson).

The following types of vesical lesions may be produced by these tumors:

a) Circumscribed single or multiple foci in the bladder wall. This type of lesion is of particular interest inasmuch as it represents an instance of distant involvement of an organ which is known to be invaded almost only by direct extension of tumor growth from the adjacent structures. By way of illustration, the discovery of 3 tumor nodes in the upper right posterior bladder wall of a patient who died of generalized lymphosarcomatosis is the only instance at this institution where the occurrence of distant bladder manifestations was observed in 1110 autopsies for malignant disease. Interestingly enough, this patient had no bladder symptoms during the course of the disease because the lesions had remained confined to the outer bladder wall and their presence was not demonstrable through the intact mucosa of the bladder cavity (fig. 6).

b) Direct invasion of the bladder by encompassing perivesical tumor masses This type of lesion was observed in 4 of our patients with lymphosarcoma A cystoscopic diagnosis was established in 2 of these patients who complained of painless hematuria and dysuria with frequency respectively In the other 2 patients, the lesions were discovered on postmortem examination

c) Extension of lymphoblastoma of the prostate into the bladder This form of bladder involvement has not been encountered in this material, however, its occurrence as a distinct entity has been emphasized by Meyer, Barney, Hunter and Heintz

d) Mucosal and submucosal hemorrhages Although not observed in this case series, it is believed that the possibility of this type of vesical involvement should be considered in determining the source of hematuria, particularly in patients with leukemia, where spontaneous hemorrhages are known to occur commonly

PROSTATE

Clinical manifestations are common in patients with lymphoblastoma of the prostate Symptoms of urinary obstruction develop as a result of rapid enlargement of the organ which may assume extensive proportions within a comparatively short period of time Sudden onset of difficulty on urination often followed by complete retention may be sometimes the first presenting symptoms of the disease (McCrea, Flaherty, Cope and Shecket, Jacobi, Panoff and Herzlich, Lubin, Fetter and Erf, Smith, etc), and the ensuing acuteness of this urological complication often dominates the clinical picture to such an extent that the possible presence of other manifestations of the disease may escape recognition By way of illustration, the following case is reported briefly

J C , a white man, aged 39, case No 43288, was admitted October 10, 1941 Two months prior to admission, the patient developed sudden urinary retention and a clinical diagnosis of carcinoma of the prostate was made at his home town Treatment consisted of suprapubic cystostomy and subsequent transurethral resection Although there was improvement of the bladder symptoms, the patient ran a continuous downhill course Physical re-examination 5 weeks later disclosed the presence of enlarged nodes in the right side of the neck Biopsy of one of these nodes revealed lymphosarcoma At the time of admission the patient was cachectic and showed evidence of generalized lymphosarcomatosis The prostate was markedly enlarged, indurate and irregular, extending into the pelvis as far as the examining finger could reach In addition, it was noted that the periprostatic tissue was studded with multiple nodules, some of which were palpable close to the rectal mucosa The patient's general condition was too poor for extensive urological investigation and since he requested to be discharged shortly after admission, he received no treatment He died 2½ months later on December 30, 1941, no autopsy was obtained Review of the tissue removed from the prostate and that from the lymph node of the neck disclosed lymphosarcoma

It is not the object of this paper to take sides in the controversy as to whether or not the prostate can be the site of the primary lesion in cases of lymphoblastoma, or whether involvement of this gland occurs only as a result of infiltration from the surrounding structures. For details regarding this problem, one should refer to the excellent contributions by Kaufman and Wright, as well as Melicow, Pelton and Fish. Suffice to say, that regardless of its source of origin, lymphoblastomatous involvement of the prostate is being recognized with increasing frequency and that one must be conscious of the possibility of its occurrence in all male patients affected by these tumors. The following case report serves as an illustration.

W. H., a white man, aged 70, case No. 11927, was admitted May 27, 1929. One month prior to admission, the patient noticed painless enlargement in the right tonsillar area. Biopsy revealed lymphosarcoma and following deep x-ray therapy, the lesion regressed. The patient remained in apparent good health until 2 months later, when he developed sudden urinary retention. A diagnosis of prostatic carcinoma was made at his home town, and the patient was subjected to suprapubic prostatectomy. He died following operation. Microscopic examination of the prostate showed lymphosarcoma.

Reports in the literature, as well as the aforementioned two case histories, suggest that the possibility of lymphoblastomatous disease of the prostate should be included in the diagnostic considerations in all patients of the younger age group (under 50 years) who present themselves with lesions resembling prostatic carcinoma. Also, in older patients who are known to have lymphoblastoma, great care must be exercised in differentiating between a new primary lesion of the prostate gland and a secondary manifestation of lymphoblastoma. Surgical intervention is not only contraindicated, but harmful in patients with lymphoblastoma of the prostate. These cases are treated best by the use of deep x-ray therapy, from which prompt relief of obstructive symptoms may be expected, at least temporarily.

TESTICLES

While the testicles may become invaded in the general spread of lymphoblastomas, most authors are in agreement that such a localization is extremely rare (Mathé, Dockerty and Priestley, Colby, etc.). The testes were the site of lymphoblastomatous lesions in 3 patients of this case series (lymphosarcoma 2, leukemia 1). Two of these 3 cases developed simultaneous bilateral involvement and interestingly enough, as in a case reported by Colby, both patients had presented themselves originally with primary manifestations in the nasopharynx which regressed following irradiation therapy. One of these cases is reported briefly:

R. K., a white man, aged 64, case No. 56479, was admitted March 27, 1946. This patient, who complained of symptoms of nasopharyngeal obstruction and occasional blood nasal discharge of 4 weeks' duration, was referred to the Roswell Park Memorial Institute with a diagnosis of lympho-epithelioma of the nasopharynx. Physical examination and blood count were not remarkable at that time except for the nasopharyngeal lesion, which regressed completely following external and interstitial irradiation However, 4 months later, the patient developed simultaneous rapid bilateral painless enlargement of the testicles and when first seen as an ambulatory patient at the urological service on August

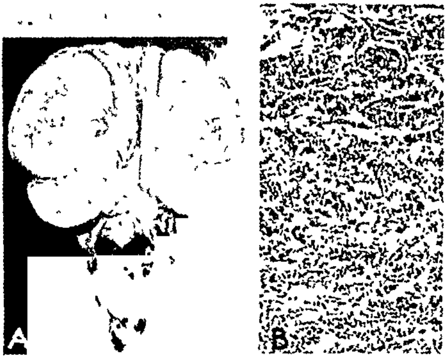


FIG. 7. *A*, replacement of right testicle and epididymis by leukemic infiltration. *B*, photomicrograph of testicle showing leukemic infiltration

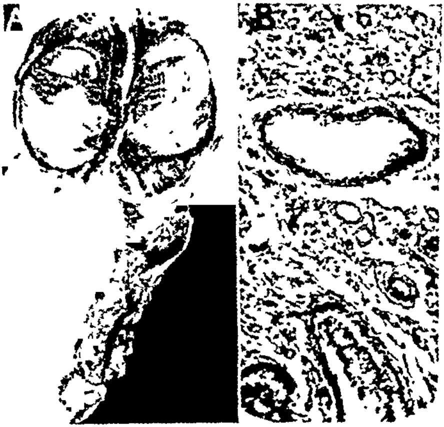


FIG 8 *A*, fibrosis of left testicle and epididymis following 432r of x-radiation *B*, photomicrograph of testicle showing fibrosis

26, 1946, both testicles were firm and smooth, measuring 8 5 by 5½ by 4.0 cm. in size. Both epididymes were involved in the process. The patient was re-admitted to the hospital for further study in October and a diagnosis of bilateral leukemic infiltration of the testicles was made after a renewed blood count revealed 106,000 leukocytes.

Removal of the right testicle (October 25, 1946) confirmed the diagnosis (fig. 7). Treatment consisted of x-radiation over the left testicle (200 k.v., 30 cm. skin target distance, 0.9 mm. Cu., H.V.L., 432 r.), which resulted in prompt regression of the organ to normal size. However, shortly afterwards, the patient developed symptoms of acute generalized leukemia with marked lymphadenopathy of the superficial lymph-bearing areas. Death occurred on November 18, 1946 and autopsy revealed diffuse leukemic infiltration of lymph nodes, lungs, nasopharynx, thyroid, heart and kidneys. Histological examination of the left testicle did not disclose evidence of leukemia, but only fibrosis (fig. 8).

A reveiw of the literature on lymphoblastomatous lesions of the testicles reveals an apparently significant number of patients with bilateral involvement. Such cases have been reported by Colby, Townsend, Hutchinson, Ewing, Dockerty and Priestley, and the fact that 2 of our 3 patients fell into this category attests the significance of this observation.

In patients who are known to suffer from lymphoblastoma, the diagnosis of testicular involvement is obvious, but in patients where a testicular lesion presents the initial manifestation of a hidden generalized disease, the condition may easily be mistaken for a primary testicular new growth. Although one may question the clinical advisability of performing an orchidectomy in patients with lymphoblastoma, it must be remembered that this operation constitutes only a minor surgical procedure. However, particularly in patients with bilateral testicular lesions, lymphoblastoma should be suspected and all diagnostic possibilities should be exhausted before orchidectomy is restored to as a therapeutic procedure.

PRIAPISM

Priapism, which occasionally may be the initial manifestation of leukemia, is a commonly known complication, nevertheless, its actual occurrence is rare. Lower and Christoferson observed it in only 2 or 0.65 per cent of 309 male patients with leukemia. A similarly low incidence was determined in our material where 1 or 0.62 per cent of 162 men with leukemia had priapism. Lowsley and Kirwin have pointed out that this type of lymphoblastomatous complication develops only in myelogenous leukemia and that it does not occur in lymphatic leukemia, lymphosarcoma and Hodgkin's disease. Since the mechanism of priapism is probably that of thrombosis of the venous spaces of the corpora cavernosa, it must be the object of treatment to relieve obstruction of the venous return flow which can be accomplished by surgical procedures or by irradiation of either the lesion or the spleen.

URETHRA

Lymphosarcoma of the female urethra has been encountered in 1 patient of this series. This very unusual case, which will be briefly reported, illustrates that even the urethra may be the site of the initial manifestation of the disease:

Mrs. M. H., a white female, aged 62, case No. 59726, was admitted April 4,

1947. The patient gave a history of intermittent spotting of 2 months' duration. She denied urinary symptoms, but stated that 2 weeks prior to admission, she noticed multiple small, painless nodules in the vulva and in the anterior vaginal wall. Biopsy of one of these nodes disclosed lymphosarcoma and the patient was referred to the Institute for treatment. Urological investigation revealed the presence of proliferative changes of the urethral mucosa, which bled on palpation and resembled caruncle (fig 9) The lesion was removed and on histological examination, lymphosarcomatous invasion of a urethral caruncle was found. The patient died 5 months later on September 23, 1947, and autopsy disclosed generalized lymphosarcomatosis with involvement of the kidneys, lungs, pancreas and lymph nodes

A similar case of urethral tumor representing the first manifestation of Hodgkin's disease has been observed by Marshall (reported in a personal communication), otherwise, as far as could be determined, no incidence of lymphoblastomatous invasion of the urethra has been reported in the literature. However, since this site of involvement may easily escape attention, its presence may be overlooked by the clinician and pathologist alike. It remains open to question, therefore, as to whether or not this type of urethral lesion may be found more often if it is being looked for, particularly in patients with generalized lymphoblastomatosis.

FIG. 9. Lymphosarcomatous involvement of urethral caruncle

EXTERNAL GENITALIA

Edema of the external genitalia may develop as a result of obstruction of the regional lymphatics in certain cases of lymphoblastoma. These changes are of only limited urological consequences, but, since they may be one of the presenting symptoms of these tumors, they are of diagnostic significance and the possibility of lymphoblastomatous disease should be included in the differential diagnosis of edematous changes of undetermined origin involving scrotum, skin of the penis or the labia.

COMMENT

A comparative study of the pathological changes produced by the various types of lymphoblastomas indicates that urologic tract involvement was most prominent and extensive in cases of lymphosarcoma, whereas it was usually less spectacular in patients with leukemia. This is illustrated by the fact that involvement of more than one part of the genito-urinary system was encountered more often in patients with lymphosarcoma where approximately 50 per cent of the cases showed lesions in more than one urologic organ. This compares with an incidence of only 16.6 per cent of multiple tract changes in the cases of the leukemia group. Interestingly enough, it was noted also that lymphosarcomatous lesions were much more invasive in nature, frequently causing a more general destruction of the organ or organs affected. In contrast, leukemic changes were frequently microscopic in character and macroscopic involvement, if present, was comprised in the majority of the cases of comparatively small and less numerous lesions. Furthermore, an apparently significant difference was determined with regard to the prevalence of the various urologic organs affected by lymphosarcoma and leukemia, namely, while lymphosarcomatous changes were demonstrable fairly often in kidney pelves (9) and ureters (8), occasionally in bladder (5), prostate (3), and testicles (2), and in one instance in the urethra, these organs were not or rarely involved in cases of leukemia (kidney pelves (2), ureters (2), penis (2), testicles (1)). On the other hand, renal involvement was much more common in leukemia (29 of 30 cases) than in lymphosarcoma (33 or 41 cases).

No reference is made to the extent and character of the changes produced in the urologic tract by Hodgkin's disease because the number of lesions observed in this case series is considered insufficient to permit conclusions.

In addition to the aforementioned urologic tract changes which occur as a direct result of tumor growth, a certain tendency to stone formation and infection may play an important role in patients with lymphoblastoma. While the secondary development of urinary calculi is observed almost exclusively in leukemia, where the uric acid level of the blood may be markedly elevated (Barney, Forkner, Merrill and Jackson, Jr.), infection may seriously complicate the clinical course in all types of lymphoblastomas. It should be emphasized in this connection that these patients have a significantly lowered resistance, and, once infection has taken place it often extends not only throughout the genito-urinary tract, but also into the adjacent structures. The following case report serves as an illustration:

L K., a white man aged 53, case No. 46830, was admitted on December 11, 1942 for x-radiation treatment of lymphosarcoma originating in the cervical lymph nodes. The patient, who remained under constant observation, was referred in fair condition to the urological service on August 22, 1944, because of rapidly developing difficulty on urination. Examination revealed almost complete retention which was caused by a small caliber stricture in the posterior urethra. The prostate was not remarkable. A few hours after dilatation of the stricture to 12 F., and evacuation of 350 cc infected residual urine, the patient had a chill and during the following days his temperature remained elevated. Five days later he developed extensive abscess formation involving the perineum, scrotum and both groins. The abscess cavities were drained by extensive multiple incisions and a perineal urethrotomy was carried out simultaneously (August

31, 1944). Nevertheless, although the temperature returned to normal and, although regression of swelling of the scrotum, perineum and groins took place, the patient did not improve. The incisions showed no tendency to heal and there was evidence of progressive necrosis in the depth of the wounds. The patient expired 6 weeks later, on October 13, 1944. Autopsy disclosed extensive pyelonephritis, ulcerative cystitis and extensive necrosis with abscess formation involving both groins and perineum.

In view of the potential seriousness of a complicating infection, it is advisable to reduce instrumentation to a minimum in these patients. In cases where urological investigation is necessary, utmost caution should be employed to avoid trauma, and antibiotics and chemotherapy alone or in combination should be given prophylactically before and after examination. Likewise, surgery should be kept to a minimum, and if necessary, it should be employed only for the treatment of emergencies which cannot be dealt with otherwise.

It is of prime importance to keep in mind that in patients who are known to have lymphoblastoma and who develop urological symptoms, one should be very reluctant to diagnose an apparently unrelated urological disease. In these cases, the possibility that one has to deal with some form of manifestation of lymphoblastomatous disease should deserve first consideration. In doubtful cases, it is suggested to withhold a final diagnosis and under these circumstances, a therapeutic test with deep x-ray therapy or nitrogen mustard may give an indication as to the type of lesion present. By using this precaution, errors of far reaching consequences can be avoided.

Close cooperation between urologist and internist is beneficial in the management of these cases, but it is also essential that the urologist is sufficiently familiar with the aspects of the lymphoblastomas in order to be able to recognize their urological manifestations.

SUMMARY

A review of 1073 cases of lymphoblastomas admitted during a 35 year period was undertaken with a view of collecting data regarding the incidence of urologic tract involvement. Four hundred and fifty-six of these patients had lymphosarcoma, 234 had leukemia and the remaining 383 had Hodgkin's disease.

Various degrees of involvement of the urologic tract organs were determined in 80 or 7.5 per cent of the 1073 cases. However, study of 143 autopsy cases revealed an incidence of 62 or 43.4 per cent which indicated that the urologic tract is actually involved much more often than clinical observation alone indicates.

Urinary tract involvement was found to be most common in lymphosarcoma and leukemia while it was comparatively uncommon in Hodgkin's disease.

The kidneys were predominantly affected but lymphoblastomatous involvement was observed also in the kidney pelves, ureters, bladder, prostate, testicles, penis and urethra.

The symptoms, clinical findings and pathological changes occurring in the genito-urinary tract as a result of involvement by lymphoblastoma are presented.

eralized malignant neoplasm, the problem lies in differential diagnosis. X-rays offer palliation. Further experience with new and to be developed radio-active isotropes may afford some relief from this distressing situation.

DR. M. M. MELICOW (New York, N. Y.): It is a great privilege to discuss Dr. Sauer's paper. I consider his contribution a noteworthy one in this rather obscure field. His review is extensive and thorough, and I am sure that everybody will find it advantageous at one time or another to refer to his article.

I would like to call attention to a unique urologic syndrome. This syndrome affects all urologists at one time or another and may be said to be both pandemic and endemic. It affects the urologist at a time when he is particularly busy and contented with his practice and work; cystoscopies have been plentiful, operations numerous and successful. God, his scalpel, and cystoscope have been good to him. Then comes a patient with apparently the usual urological complaints who does not show any improvement following the routine urologic work-up and treatment. The condition may be a "perinephric abscess" that refuses to heal, a "ureteral stricture" that goes bad following treatment or "prostatitis" that becomes worse with massage or operation.

The early symptoms of this syndrome are impatience and irritation on the part of the urologist. Then comes the blow. A piece of tissue or exudate or a postmortem report shows "lymphosarcoma" or "Hodgkin's disease". The syndrome reaches its height when the urologist is heard to say 'I should have thought of it'. There are no more sad words than 'I should have thought of it', in medicine.

I believe we are indebted to Dr. Sauer for having presented us with this thorough study. Reading this article will immunize us against this syndrome.

Now, as to lymphoblastomas: one may classify them as follows:

1) Lymphosarcomas: These are sarcomas of lymph glands. They can metastasize or be multi-centric in origin. They may metastasize to the urinary tract, or invade an adjacent urinary tract organ from a local focus.

2) Lymphatic leukemia: This is a circulating lymphosarcoma

3) Leukemic infiltrations are the colonies from a lymphatic leukemic or a lymphosarcoma.

4) Hodgkin's disease in a form of lymphosarcoma except that it involves the reticulum cells.

In a hurried review of our cases, I noted that the pyelograms presented several common features which may be characteristic of metastatic malignancy to the kidney. The organ appears to be either uniformly or asymmetrically enlarged while the pyelogram reveals no significant abnormality except an elongation of some of the infundibula of the calyces. This is in contradistinction to the compression, elongation and curvature of the calyces which one sees in early clear cell carcinoma and cysts, and obliteration of the calyces in the more advanced cases or in the granular-cell carcinomas.

Four slides were shown: 1) lymphosarcoma of kidney; note infiltration of cancer cells between glomeruli and tubules; 2) lymphosarcoma of prostate; 3) metastatic lymphosarcoma of testis; note cancer cells surrounding and compressing tubules; 4) multiple myeloma invading testis.

DR. THOMAS E. GIBSON (San Francisco, Calif.): (Slide). It is important that urologists be familiar with the clinical manifestations of lymphosarcoma and lymphoid tumors because of their frequent involvement of the genito-urinary tract.

There are four different ways in which lymphosarcoma or lymphomata may involve the kidney. They are shown graphically in this slide.

(Slide) The first is the capsular or perirenal type, in which the kidney is surrounded by a tumor mass. Secondary invasion of a kidney may occur from any direction. The ureter may be surrounded by the mass, causing renal colic and hydronephrosis. Invasion of the kidney may occur from any point in the perimeter.

The second shows a multiple nodular type of involvement.

The third shows the diffuse interstitial type of infiltration.

The fourth shows involvement of the kidney by a single large tumor; lymphoma of the kidney are probably never primary; however, types 1 and 4 may simulate primary renal neoplasms and even at operation no involvement elsewhere may be found. Such a case is shown in the next slide.

(Slide) This is a pyelogram which shows a defect typical of almost any renal tumor.

(Slide) This is a drawing of the tumor removed by nephrectomy, which weighed four and a half pounds. I did not realize until after the mass was removed that I was not dealing with a primary tumor of the kidney. As you see, this is type 1, which illustrates clearly the simulation of primary tumor of the kidney.

In 9 cases in which nephrectomy has been done in this type of case, 6 died within 1 year. Results in 3 unknown.

One report of 650 tumors reports five as lymphosarcoma, and considered none of them as being primary.

Dr. Ernest M. Watson (Buffalo, N. Y.): After a general, quick once-over of this subject, what we get out of it—we get the fun of working with good pathologists who, after all, are the most important members of this team. They have led us to a higher level of appreciation of what the structure is in this particular process, which includes these three divisions of lymphatic disease. Now, without the help of the pathologist, we are somewhat lost, and we are sometimes led astray, even with his help.

What do we learn? We learn that an accuracy of diagnosis, a more searching effort to separate lymphoblastomas from other processes, is certainly worth while. Some of our cases had unnecessary surgery, and that is not too serious a blunder, but maybe in the future it is well for us to bear in mind that we don't want to repeat that too frequently.

One of our cases had a prostate removed for carcinoma and it was not carcinoma but lymphosarcoma.

Most of these distortions of the pyelographic picture are due to pressure and to involvement of the renal parenchyma from the outside; others from isolated areas inside that give distortion, and a few from lesions—growing in the bladder wall. Then, of course, there are infections.

Probably the best we can gain from a study like this is to have more effort made on diagnosis and realizing that the clinical symptoms can be hematuria, pain, evidences of back pressure, and anything else that causes dysfunction in the upper and lower urinary tract.

eralized malignant neoplasm, the problem lies in differential diagnosis. X-rays offer palliation. Further experience with new and to be developed radio-active isotropes may afford some relief from this distressing situation.

Dr. M. M. Melicow (New York, N. Y.): It is a great privilege to discuss Dr. Sauer's paper. I consider his contribution a noteworthy one in this rather obscure field. His review is extensive and thorough, and I am sure that everybody will find it advantageous at one time or another to refer to his article.

I would like to call attention to a unique urologic syndrome. This syndrome affects all urologists at one time or another and may be said to be both pandemic and endemic. It affects the urologist at a time when he is particularly busy and contented with his practice and work; cystoscopies have been plentiful, operations numerous and successful. God, his scalpel, and cystoscope have been good to him. Then comes a patient with apparently the usual urological complaints who does not show any improvement following the routine urologic work-up and treatment. The condition may be a "perinephric abscess" that refuses to heal, a "ureteral stricture" that goes bad following treatment or "prostatitis" that becomes worse with massage or operation.

The early symptoms of this syndrome are impatience and irritation on the part of the urologist. Then comes the blow. A piece of tissue or exudate or a postmortem report shows "lymphosarcoma" or "Hodgkin's disease". The syndrome reaches its height when the urologist is heard to say 'I should have thought of it'. There are no more sad words than 'I should have thought of it', in medicine.

I believe we are indebted to Dr. Sauer for having presented us with this thorough study. Reading this article will immunize us against this syndrome.

Now, as to lymphoblastomas: one may classify them as follows:

1) Lymphosarcomas: These are sarcomas of lymph glands. They can metastasize or be multi-centric in origin. They may metastasize to the urinary tract, or invade an adjacent urinary tract organ from a local focus.

2) Lymphatic leukemia: This is a circulating lymphosarcoma

3) Leukemic infiltrations are the colonies from a lymphatic leukemic or a lymphosarcoma.

4) Hodgkin's disease in a form of lymphosarcoma except that it involves the reticulum cells.

In a hurried review of our cases, I noted that the pyelograms presented several common features which may be characteristic of metastatic malignancy to the kidney. The organ appears to be either uniformly or asymmetrically enlarged while the pyelogram reveals no significant abnormality except an elongation of some of the infundibula of the calyces. This is in contradistinction to the compression, elongation and curvature of the calyces which one sees in early clear cell carcinoma and cysts, and obliteration of the calyces in the more advanced cases or in the granular-cell carcinomas.

Four slides were shown: 1) lymphosarcoma of kidney; note infiltration of cancer cells between glomeruli and tubules; 2) lymphosarcoma of prostate; 3) metastatic lymphosarcoma of testis; note cancer cells surrounding and compressing tubules; 4) multiple myeloma invading testis.

Dr. Thomas E. Gibson (San Franciso, Calif.): (Slide). It is important that urologists be familiar with the clinical manifestations of lymphosarcoma and

The effect of the detergents is remarkable, especially that of tergitol 4. However, it is quite possible that with other stones, results will differ. Most of the stones used were the relatively soft, new calcium phosphate stones removed from kidneys of paraplegics at Hines Veterans Administration Hospital, Hines, Illinois. These experiments have led us to believe that some stones of the bladder and of the kidneys may be dissolved by irrigations with the proper detergent-acid solution. Because the toxicity of tergitol 4 has been previously determined[7,8] and it has been used by Brantigan,[9,10,11] and the author, as an irrigating solution of the pleural cavity in empyema with excellent results, a clinical trial at present is being undertaken. Abrahamson[12] reports the successful dissolving of 9 of 10 bladder stones with Suby's solution. However, this solution has not been successful in our hands. In fact, we have had stones develop in patients on tidal drainage using Suby's, to which has been added one of the new cationic detergent antiseptics, as the irrigating solution.

TABLE 1

ACID	A	B	O
0.1 N HCl	0.5	6.0	48.0
0.01 N HCl	2.0	12.0	72.0
2% acetic	2.1	24.0	72.0
¼% acetic	6.1	48.0	144.0
1% citric	72.0	156+	156+
1% phosphoric	104.0	156+	156+

Figures represent hours.

Note: 1) The stones used were approximately 1 cm. in diameter in all cases. 2) One hard, old staghorn calculus measuring 4 by 3 by 2 cm. was dissolved in 8 days' exposure to a continuous drip of ¼ per cent acetic and 1:3000 tergitol.

One other interesting observation was made during these experiments. In all cases when the stone was dissolved, the inorganic salts were dissolved out of the stone, leaving a matrix of organic debris. If the solution were left undisturbed, an apparently intact stone would be found floating on the surface of the solution. Agitation immediately converted this matrix to flakes of pus as seen in the urine of pyelitis. The detergent apparently acted by enabling the acid solvent to penetrate through the concentric layers of pus and thus dissolve the inorganic salts that make up these stones. In the plain acid solutions, the coating of pus could be seen to have swollen and the stones became shaggy after prolonged exposure, thus achieving a water tight barrier or making the dissolving process extremely slow.

The application of detergents to the problem of the dissolving of stones is only one of the many uses that immediately come to mind.

[7] Smyth, H. F. Jr. and Seaton, J.: J. Indust. Hyg. & Toxicol., 23: 259, 1941.
[8] Freeman, S., Burrill, M. W., Li, T. W. and Ivy, A. C.: Gastroenterology, 4: 332, 1945.
[9] Brantigan, O. C. and Owings, J. C.: Bull. School of Med., Univ. of Md., 26: 247, 1912.
[10] Tonolla, E. H. and Brantigan, O. C.: Diseases of Chest, 13: 123, 1947.
[11] Brantigan, O. C. and Rigdon, H. L.: J. Thoracic Surg., 16: 416, 1947.
[12] Abramson, D. J.: J. Urol., 58: 29, 1947.

The problem of urethritis, especially chronic, nonspecific urethritis, might be aided if a detergent were incorporated into the local medicines used, to carry the medicine through pus and mucus to the depths of the periurethral glands. The fact that the invert soaps, usually quarternary ammonia derivatives, are also excellent antiseptics, warrants immediate investigation of their possibilities in both male and female gonorrhea and as prophylactics against venereal disease. Their physical properties indicate that they should be much more efficacious and simple to use than the cumbersome, time-consuming and frequently irritating methods of prophylaxis in vogue today.

Combinations of detergents and biologicals may be of use in prostatitis and cystitis by instillation, the detergent being of two-fold use as a vehicle to carry the biological into the depths of the glands and also to facilitate drainage of the glands by dissolving pus in the ducts.

There is no doubt that detergents will be of great value in the treatment of pyelitis. Renal lavage with a detergent should dissolve the pus and minimize renal damage caused by ureteral blockage.

Lest enthusiasm override caution it should also be mentioned that Cooper[13] reports excellent results using strong solutions of detergents in sclerosing varicose veins.

SUMMARY

A brief review of the various types of detergents has been presented.

The in vitro results of using various detergents to dissolve kidney stones have been reported.

Other possible uses of detergents in urology were suggested and briefly discussed.

The author wishes to express his appreciation for advice and encouragement to Dr. Knowlton E. Barber, associate professor of urology, Northwestern University Medical School, and consultant in urology, Hines V. A. Hospital, Hines, Illinois.

---

[13] Cooper, W. M.: Surg., Gynec. & Obst., 83: 647, 1946.

THE JOURNAL OF UROLOGY
Vol 61, No 3, March 1949
Printed in U S A

A CLINICAL STUDY OF A NEW SULFONAMIDE (NU-445) IN THE TREATMENT OF URINARY TRACT INFECTIONS

JOSEPH A. LAZARUS AND LEWIS H. SCHWARZ, B S.

Any agent employed in therapeutics should be distinguished, above all, by clinical efficacy and safety. By these criteria, the value of most of the sulfonamide preparations employed in the treatment of urinary tract infections leaves much to be desired since the tolerance of some patients for these drugs is low, and because they are too frequently of no avail, particularly in conditions due to gram-negative organisms

Sarnoff, et al.[1], have recently reported encouraging results with a new sulfonamide, designated NU-445, which they studied clinically in 14 cases of B. proteus infections of the urinary tract. This drug, which is chemically 3,4-dimethyl-5-sulfanilamido-isoxazole, was evaluated experimentally by Schnitzer and coworkers[2]. These investigators state that NU-445 "possesses remarkably good solubility over a wide pH range, particularly in the physiologically important range of pH 6.0–8.0". Obviously, this property greatly reduces the likelihood of crystalluria and deposition of crystals within the urinary tract. Pertinent animal experiments carried out by Schnitzer, et al. proved this point They also demonstrated that the therapeutic potentialities of the new drug, as judged by in vitro tests and by experimentally induced infections, "compare favorably with those of known and clinically useful sulfonamides". In view of these gratifying findings, and because of the limitations of other sulfonamides in the field of urology, it was decided to investigate the therapeutic value of the new compound.

CASE MATERIAL

NU-445 was administered to 25 patients with urinary tract infections: 19 males, ranging in age from 17 to 73 years, and 6 females whose ages ranged from 32 to 65 years. For these patients, the following diagnoses had been established:

	cases
Acute cystitis	5
Pyelitis and prostatitis	1
Pyelocystitis	2
Pyelonephritis	4
Prostatitis	2
Benign prostatic hypertrophy	7
Pyonephrosis	2
Hydronephrosis and hydroureter	1
Pyoureter and pyelitis	1

These 25 cases, of which 18 were unmixed infections involved seven groups of organisms, namely: A. aerogenes, B. pyocyaneus, E coli, P. morganii, P. vulgaris, Staph. aureus, and Strep. hemolyticus. Counting each of the offenders of the mixed infections separately, there was a total of 33 infections.

---

[1] Sarnoff, S. J., Friedman, M. A. and Hyman, A. A. The treatment of Bacillus proteus [illegible]

[2] [illegible]-Hoo, G., Mangieri, C. N and Roe, M. D.: Pharmacological and chemotherapeutic properties of 3,4-dimethyl-5 sulfanilamido-isoxazole J Pharmacol & Exper. Therap, 88: 47–57, 1916.

In 2 of the cystitis cases, there was prostatic involvement, one having an associated prostatitis and the other a prostatic hypertrophy. Similarly, one of the pyelocystitis cases and one of the pyelonephritis cases was complicated with prostatitis. One patient with pyonephrosis had an accompanying cystitis. The prostatitis of 1 case was associated with vesiculitis. A diverticulum of the bladder was found in one of the two patients with pyelocystitis. Finally, in 2 cases of pyelonephritis, one of which had an accompanying cystitis, and in one case of pyonephrosis, the inflammatory process was complicated with lithiasis.

PROCEDURE

NU-445[3] was administered orally to all 25 patients and, in addition, 8 of these patients were treated with bladder instillations.

Various dosage plans were followed, depending on the severity of symptoms and the response obtained. Thus, five patients received 1 gm. (2 tablets) q 4 hours for 4 doses daily and, in one of them, the individual dose was increased after 6 days to 2 gm. given at the same intervals; 9 patients were placed initially on the latter plan and for 4 of them, the daily dose was heightened after several days by either giving 4 gm. q 4 hours for 4 doses or by administering 2 gm. q 2 hours for 8 doses daily; for 11 patients, the latter schedule was prescribed initially. Thus, the oral daily dose varied from 4 gm. to 16 gm. The medication was continued over periods of time ranging from 1 to 140 days with an average of 25 days. The smallest total amount administered to one patient during the entire period of treatment was 16 gm. and the maximum quantity ingested by one individual was 1680 gm. (!) with an average total intake of 259 gm. per patient. However, in the majority of cases, the total dose administered ranged from 100 to 150 gm.

In general, at least 3 successive negative cultures were required before termination of treatment. Cures were assumed if the urinary cultures remained negative for 2 months following discontinuation of the drug.

In 8 patients, the oral medication was supplemented by bladder instillations: The bladder was first thoroughly irrigated with a 2 per cent solution of boric acid and this was followed by the instillation of 20 cc of a sterile 10 per cent solution of the lithium salt of NU-445[3]. In 7 instances, these treatments were given once a week for periods ranging from 4 to 25 weeks. One case received 35 instillations: Initially, 8 treatments were given on subsequent days and then 27 instillations at semiweekly intervals. The local applications were initiated either concurrently with or at termination of the oral medication.

For all patients, routine urine analyses and hemograms were done at frequent intervals. Moreover, the renal elimination of NU-445 was studied for 8 patients. These determinations were carried out in 24 or 48 hour urine specimens. In 2 instances, only one such specimen was studied and for the other 6 persons, the number of specimens ranged from 2 to 7. The total daily doses ingested by these patients were 4 to 8 gm. In addition, for one of these subjects, the individual voidings over a 24 hour period were examined at a time when his daily intake of NU-445 had been increased to 16 gm. The chemical technique was that of Bratton and Marshall as described in Technical Manual 8-227 issued by the War Department. Smears of the urinary sediment were examined frequently. Similarly, bacteriological cultures were studied at frequent intervals. These cultures were obtained by transferring sediments of urines derived from the bladder or the kidneys to suitable media.

---

[3] The NU-445 was generously supplied by Dr. Leo A. Pirk of Hoffmann-La Roche, Inc., Nutley, New Jersey.

CLINICAL RESULTS

Table 1 shows the results obtained with NU-445 in the 18 cases of unmixed infections due to five types of organisms. The findings were as follows: Bacteriological reversal was achieved in 10 patients; 1 case was classified as equivocal because the infection recurred 8 weeks after discontinuation of therapy; and in 7 cases, the urinary culture remained positive.

TABLE 1. *Distribution of pathogenic organisms in 18 patients with unmixed infections of the urinary tract and results of treatment with NU-445*

TYPES OF ORGANISMS	NO. OF INFECTIONS	CURES	FAILURES	EQUIVOCAL RESULTS
A. aerogenes............	2	1	1	
B. pyocyaneus..........	5	2	3	
E. coli..................	8	5	2	1
P. vulgaris............	2	2		
Staph. aureus...........	1		1	
	18	10	7	1

Table 2 shows the results obtained with NU-445 in the 7 patients afflicted with more than one organism and involving a total of 15 single infections. These were due to five types of offenders. The signs in the vertical columns representing the 7 cases are correlated with the pathogenic organisms afflicting a given patient. A plus sign indicates that NU-445 was effective against the offender with which it is correlated, and a minus sign that the drug was of no avail. As the symbol for an equivocal result, a question mark was chosen. The results in these mixed cases were as follows: In 3 patients, NU-445 eliminated both offenders. Similarly, both organisms disappeared from the urine of 1 patient (M. B.) after he had received, on one day, 16 gm. of the drug, but the infection recurred 2 weeks following discontinuation of therapy. This case was classified as equivocal because the treatment was considered to have been incomplete. In each of 2 other patients afflicted with 2 pathogenic organisms, one of the offenders was eradicated but the other persisted. Finally, of the 3 offenders of 1 case, 2 were eradicated but the urine remained positive for the third organism.

Thus, of the total group of 25 cases studied, 13 patients, or 52 per cent, were cured; results in 2, or 8 per cent were equivocal; and in 10, or 40 per cent, the urine remained infected with one organism.

A summation of the results, [illegible] the unmixed and mixed infections, is given in table 3 in which each off [illegible]nism is counted as a separate infection. It can be seen that of the total of 33 infections, the pathogenic organisms were eradicated in 20 instances, or 60.6 per cent; that results were equivocal in 3 cases, or 9.1 per cent; and that NU-445 failed to eliminate the offender in 10 instances, or 30.3 per cent.

A brief discussion of the cases recorded as failures follows: The patient with the unmixed Staph. aureus infection received 16 gm. of NU-445 daily for 3 days, and did not tolerate such massive doses. Treatment was discontinued but it is realized that this has not been a fair trial. Similarly, the negative result in one of the infections due to A. aerogenes may have been attributable to inadequate treatment. Administration of NU-445 for 9 days was attended by sterilization of this patient's urine. When the infection recurred 2 weeks later, the drug was reinstituted, but was discontinued after 9 days because of a change in the blood picture which may or may not have been due to the drug.

TABLE 2. *Distribution of pathogenic organisms in 7 patients with mixed infections of the urinary tract and results of treatment with NU-445.*

TYPES OF ORGANISMS	PATIENTS						
	S.L.	M.R.	E.S.	E.G.	I.A.	K.S.	M.B.
B. pyocyaneus	+	+	+	+	+	−	
E. coli	−			+	+	+	?
P. morganii		+					
Staph. aureus			−				?
Strep. hemolyticus			+				

TABLE 3. *Distribution of pathogenic organisms in 25 patients with urinary tract infections counting each organism separately and results of treatment with NU-445*

TYPES OF ORGANISMS	TOTAL NO. OF INFECTIONS	CURES	FAILURES	EQUIVOCAL RESULTS
A. aerogenes	2	1	1	
B. pyocyaneus	11	7	4	
E. coli	13	8	3	2
P. morganii	1	1		
P. vulgaris	2	2		
Staph. aureus	3		2	1
Strep. hemolyticus	1	1		
	33	20	10	3

Two of the failures, an unmixed infection due to B. pyocyaneus and the one patient afflicted with three pathogens of which the Staph. aureus resisted to treatment, were complicated with bilateral renal calculi. Also unaffected by NU-445 medication was the patient with the diagnosis of hydronephrosis and hydroureter. This patient presented an unmixed infection due to B. pyocyaneus. Another failure was the patient with the diverticulum of the bladder. His urine yielded B. pyocyaneus and E. coli of which the latter pathogen was not eradicated by the drug. Finally, among the cases not responding to treatment were three instances of prostatic hypertrophy. Two of these were unmixed infections due to E. coli and one a mixed infection due to B. pyocyaneus and E. coli of which the former organism failed to respond to treatment. Thus, the infections of all these latter 7 cases were associated with pathological findings productive of urinary stasis or obstruction. Under these anatomical conditions, eradication of an infection is most difficult to achieve.

Of particular interest are the results obtained against B. pyocyaneus and E. coli because these are the pathogens which were most frequently encountered in the group of cases presented. Therefore, the findings have more significance than those pertaining to the other organisms subjected to the action of NU-445.

B. pyocyaneus. This bacillus, which was present in 11 instances, was isolated from urine derived from the bladder alone in 5 cases; from urine derived solely from the right kidney in 1 instance; and from both the bladder and the kidney urines in 3 cases. In 2 patients, the organism was present in the blood stream. In one of the bacteremia cases, the pathogen was found in the lower and upper urinary tract and in the other only in the bladder.

NU-445 was effective in eradicating the organism from the bladder in 6 cases and failed to sterilize the urine from this organ 4 times. One of the cures was attributed to bladder instillations of NU-445 which were applied after massive oral doses had been ineffectual. However, among the failures is a case which did not respond to local instillations. Of the total of 5 renal urinary cultures positive for B. pyocyaneus, 4 were rendered negative. The blood stream was sterilized in both cases in which it was infected. Thus, of the 11 B. pyocyaneus infections, cures resulted in 7 instances, or 63.6 per cent.

E. coli. This organism, which was present in 13 instances, was isolated solely from the bladder urine in 11 cases and from urine derived both from kidneys and bladder in 1 instance. In 1 patient there was a concomitant infection of the blood stream. NU-445 was effective in eradicating the pathogen from the bladder in 8 cases, and failed to do so 3 times. In 3 patients the cures were attributed to bladder instillations rather than to the oral administration of the drug. In 2 instances results were equivocal; in 1, because of insufficient dosage and in the other, because the infection recurred 8 weeks after discontinuation of the drug. The renal urine from the patient whose kidneys were affected was sterilized, as was the blood stream in the patient with bacteremia. Thus, of the 13 E. coli infections, cures resulted in 8, or 61.5 per cent.

All other infections were treated in such small numbers that the percentwise expression of results would be meaningless. However, the general trend of findings appears from table 3.

Tolerance. NU-445 was tolerated without severe complications except for the aforementioned 2 cases in which the drug was discontinued because of presumed untoward effects. In 1 of these patients, the medication was stopped because of a concomitant rise of blood pressure, and in the other because of the development of a slight leukopenia (the leukocyte count dropped from 8,600 per cu. mm. to 4,600 per cu. mm.) and a decrease in the hemoglobin concentration (from 93 per cent ((Leitz)) to 67 per cent). The daily intake of both these patients was 16 gm. and the total quantities which had been ingested by them at the time of the appearance of the reactions were 50 gm. and 300 gm. respectively. Since both subjects refused reinstitution of treatment with NU-445, the question remains open whether the blood pressure rise and the change in the hemogram were actually related to the administration of the drug. Thirteen patients tolerated as much as 16 gm. a day without serious complications. In fact, of these 13 subjects, 6 experienced no untoward reactions whatever, and this is remarkable if one considers that one of them received as much as a total dose of 1176 gm. given over a period of 77 days. The one patient who took an even larger total dose; namely, 1680 gm. over a period of 140 days, complained of frontal headache, flushing of the face, and flatulence. These reactions were extremely mild and were observed occasionally in the course of treatment by many patients. There was no case of gastro-intestinal sensitivity. Skin reactions occurred in three instances (pruritus and a mild rash in one patient and pruritus in two others). Complaints of similarly little significance were vertigo in 1 case, tingling sensations in 4 instances, and generalized malaise in 2 cases.

Crystalluria, a frequently observed concomitant of therapy with other commonly used sulfonamides, was conspicuous by its absence in all 25 patients. Furthermore, there was no evidence of deposition of crystals in the urinary tract or of hematuria on repeated microscopic examination of the sediments. This freedom from damage to the urinary tract is remarkable since NU-445 was administered without adjuvant alkali and since fluid intake was not forced.

Treatment with other urinary tract agents. Prior to the initiation of treatment with NU-445, several of the patients had received other medication which failed to sterilize their urine. Thus, sulfadiazine had been tried without avail in seven infections due to B. pyocyaneus, and in one infection due to E. coli. The former organism was eradicated by NU-445 in 4 instances. Streptomycin failed to eliminate B. pyocyaneus in 6 instances and E. coli in 2. In contrast, NU-445 proved effective against the former bacillus in 4 cases, and against the latter in one instance.

URINARY EXCRETION STUDIES[4]

The total amounts of NU-445, as determined for 8 patients in their 24 and 48-hour urine specimens, are given in the column to the extreme right of table 4. Correlated with the values for the total renal elimination are the daily doses of NU-445 ingested, the total volumes of the 24 or 48 hour specimens, and the concentrations of free and acetylated NU-445 expressed in mg. per cent.

The figures recorded show that the total quantities of the drug excreted in 24 hours after a daily intake of 4 gm. ranged from 0.98 gm. to 4.11 gm. The amounts eliminated within 24 hours, following a daily dose of 8 gm., varied from 1.63 gm. to 8.8 gm., and those after the same daily dose excreted within 48 hours ranged from 6.9 gm. to 15.7 gm. Thus, there exists, in general, correlation between the ingested amounts of NU-445 and the quantities excreted. Furthermore, if the amounts eliminated by a given patient within the individual periods of collection are correlated with the volumes of urine, it appears that there is a close relationship between the quantities of NU-445 excreted and the volumes of the urines. For example, the smallest total amount of NU-445 determined for patient W.L.; namely, 0.98 gm., was found in the 24 hour urine specimen representing the smallest volume (474 cc) and the specimen representing the largest volume (947 cc) yielded the greatest quantity of NU-445; namely, 4.11

---

[4] We are indebted to Dr. R. J. Schnitzer and Mr. W. L. Schleyer of Hoffmann-La Roche, Inc., Nutley, N. J., for carrying out the urinary determinations and to the former for assisting us in the interpretation of the laboratory findings.

TABLE 4. *Urinary excretion of NU-455 determined in 24 and 48 hour urine specimens for 8 patients receiving NU-445*

PATIENT	DAILY DOSE OF NU-445	PERIOD OF URINE COLLECTION	VOLUME OF URINE	EXCRETION OF NU-445		AMOUNTS OF NU-445 EXCRETED
				Free	Acetylated	
	gm.	*hours*	*cc.*	*mg. %*	*mg. %*	*gm.*
E. A.	4	24	4700	28	20	2.26
	8	24	4500	54	38	4.14
W. L.	4	24	500	195	79	1.37
	4	24	947	240	195	4.11
	4	24	591	236	80	1.87
	4	24	474	148	59	0.98
	4	24	948	228	99	3.10
	4	24	710	200	136	2.38
	4	24	888	172	102	2.42
I. P.	8	24	1776	293	127	7.45
	8	48	2900	305	89	11.4
	8	48	2910	375	165	15.7
	8	48	3700	270	120	14.4
E. G.	8	24	2800	176	28	5.8
	8	24	1361	320	170	6.7
	8	24	1380	236	104	4.7
	8	24	2020	160	90	5.1
	8	24	1610	270	130	6.4
B. C.	8	24	740	178	30	1.63
	8	48	4320	120	40	6.9
	8	48	4100	130	66	8.0
A. W.	7	48	2750	120	76	5.39
M. R.	4	24	1200	208	74	3.4
M. M.	8	24	890	300	190	4.4
	8	24	946	700	30	8.8
	8	24	770	750	280	7.9
	8	24	890	600	320	8.2
	8	24	770	680	300	7.9

[illegible] The average concentration of NU-445 [illegible]

[illegible] from Table 5 that the amounts of the drug eliminated by the

TABLE 5. Total intake and total urinary elimination of NU-445 as calculated from the excretion findings reported for 8 patients in table 1

PATIENT	[illegible]	[illegible]	TOTAL AMOUNTS OF NU-445 EXCRETED		RATE OF ACETYLATION OF NU-445 IN % OF ELIMINATED AMOUNTS
	gm.	cc.	gm.	%	
[illegible]	[illegible]	[illegible]	6.4	52.5	[illegible]
[illegible]	[illegible]	[illegible]	4.3	[illegible]	31.5
	One sample missing				
	[illegible]	[illegible]	7.9	55.5	31.7
[illegible]	[illegible]	[illegible]	42.9	87.3	28.3
[illegible]	[illegible]	[illegible]	22.7	72.0	33.0
B. C.	[illegible]	[illegible]	16.5	41.0	26.5
[illegible]	[illegible]	[illegible]	5.4	35.5	29.0
[illegible]	4	1200	2.4	55.0	26.2
M. M.	[illegible]	[illegible]	27.2	23.0	30.0
Average				63.5%	30.1%

TABLE 6. Urinary excretion of NU-445 determined in 16 specimens collected individually over a 24 hour period for patient B.C. receiving a daily dose of 16 gm. of the drug

SPECIMEN NUMBER	VOLUME OF URINE	EXCRETION OF NU-445		AMOUNTS OF NU-445 EXCRETED	RATE OF ACETYLATION OF NU-445 IN % OF ELIMINATED AMOUNTS
		Free	Acetylated		
	cc.	mg. %	mg. %	gm.	
1	115	200	100	0.345	33.0
2	50	240	170	0.255	33.0
3	185	78	22	0.185	22.0
4	185	176	48	0.415	21.0
5	180	110	20	0.235	15.4
6	175	140	36	0.308	20.5
7	33	300	160	0.152	35.0
8	180	270	80	0.630	23.0
9	175	300	130	0.752	30.0
10	125	528	112	0.800	17.5
11	145	468	212	0.986	31.0
12	90	324	156	0.430	33.0
13	170	318	242	0.930	43.0
14	175	348	162	0.890	32.0
15	175	450	230	1.180	34.0
16	24	318	182	0.112	36.0
Total					
Average					

individual subjects ranged from 38.6 per cent to 93 per cent of the quantities ingested during the same period, with an average total excretion of 69.5 per cent. These figures do not include any portions of NU-445 excreted on subsequent days without medication and, therefore, they do not represent a complete balance. Furthermore, it appears from table 5 that approximately 30 per cent of the eliminated quantities were present in the form of the acetyl compound of NU-445. These figures demonstrate that the drug is excreted promptly in high percentage by the kidneys and that the rate of acetylation is low.

The amounts of NU-445 determined for one of the patients in each of 16 specimens collected separately over a 24 hour period are recorded in table 6. It appears that the total elimination was 8.6 gm., or 54 per cent of the daily dose (16 gm.). The findings show that the amounts of NU-445 eliminated in the individual voidings differ greatly from each other. Therefore, the rate of the drug's excretion must be determined in 24 hour specimens and not in a single voiding.

SUMMARY AND CONCLUSIONS

The effectiveness of a new sulfonamide, 3,4-dimethyl-5-sulfanilamide-isoxazole (NU-445) was studied in 25 cases of urinary tract infections involving seven groups of pathogenic organisms. There were 18 cases with unmixed and 7 cases with mixed infections. Counting each of the offenders separately, there was a total of 33 infections, the majority of which were due to B. pyocyaneus or E. coli.

NU-445 was administered orally to all 25 patients and, in addition, eight of these subjects were treated with bladder instillations. The daily oral dose varied from 4 to 16 gm. and the average duration of treatment was 25 days. One patient received as much as 1680 gm. over a period of 140 days and the average total intake per patient was 259 gm.

Results were as follows: The infecting organisms were eradicated in 20 instances, or 60.6 per cent; NU-445 was ineffective in 10 instances, or 30.3 per cent; and results in the remaining three infections were equivocal.

The high incidence of positive responses to treatment with NU-445 in Pyocyaneus and coli infections is remarkable. The drug proved effective in cases in which sulfadiazine and/or streptomycin had failed to eradicate these pathogens.

The good solubility of NU-445 obviates the need for concomitant alkali medication even if very large doses are administered. In none of the cases studied was crystalluria or hematuria observed. Similarly, there was no evidence of deposition of crystals in the urinary tract. In general, NU-445 was tolerated without serious complications. Discontinuation of treatment became necessary, however, on account of untoward effects in two instances.

Urinary excretion studies revealed that NU-445 is eliminated promptly.

It is concluded that the new drug is a valuable adjuvant in the treatment of urinary tract infections caused by B. pyocyaneus and E. coli.

875 Park Ave., New York, N. Y.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

FURTHER STUDIES RELATIVE TO THE TREATMENT OF URINARY TUBERCULOSIS BY CHEMOTHERAPY[1]

GEORGE E. SLOTKIN

From the Department of Urology, School of Medicine, University of Buffalo, the Millard Fillmore Hospital and E. J. Meyer Memorial Hospital, Buffalo, N. Y.

AND

WILBERT SPENCER, PH.D.

From the Department of Bacteriology, University of Buffalo and the Millard Fillmore Hospital

Some 9 months ago an idea was conceived for a new and more rapid control of urinary tuberculosis than had heretofore existed; at approximately full term we wish to report the results obtained in the original cases, and to add many more in which variations of the therapy were introduced, all with the same satisfactory results.

Sufficient time has elapsed to evaluate the method of treatment, to control the results by re-examination and to confirm the results in these early cases with a group of cases of various other types of genito-urinary tuberculosis.

As our investigations proceeded and the results were analyzed, and as stated in our original presentation, we did not try to create the impression that the last word had been written, but rather that here was simply an opening wedge in the treatment of this devastating condition and that other or additional combinations might prove to be of more value or facile in their administration.

The problem of the treatment of tuberculosis by synergistic therapy has been a matter of investigation and reported by others. Wilbolz, at a meeting of this Association in Chicago, reported the 10 year results in 660 nephrectomies, with 40 per cent mortality from disseminated tuberculosis of the lungs or other organs. In his conclusions he stated "that we must search for methods by which we may be able to enhance the natural tendency toward healing. This may be found eventually by chemical or physical means. Perhaps at some future time we may find a way of healing tuberculosis of the urinary tract without the sacrifice of the kidney."

Calloman, Kolmer, Rule and Paul, investigating the synergistic action of streptomycin and one of the sulfones, diasone, reported striking results upon their in vitro studies but unfortunately the clinical results were valueless.

Petter and Prenzlau, in the treatment of a large group of pulmonary cases with diasone and streptomycin, reported satisfactory results to a considerable degree.

Smith, McCloskey and Emmart were enthusiastic with the use of promin and streptomycin, although the sulfone was very toxic, and stated that their investigations were continued in the search for an additional combination which they know must exist; recently Lincoln, Kirmise, and DeVito reported their results in 7 cases of tuberculous meningitis, usually a fatal disease, in which streptomycin and promizole were utilized with striking results in 5 patients who are living and well.

---

[1] Read at annual meeting, American Urological Association, Boston, Mass., May 18, 1948.

Finally, S. A. Waksman, who gave us streptomycin, in a recent address stated that "the most significant of the factors and problems of the clinician is the development of resistance of the tubercle bacillus to streptomycin. In order to overcome these limitations an intensive search must be made for other agents that will be more effective, alone or combined, with streptomycin. The com-

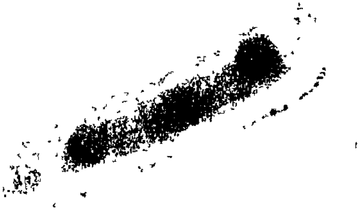


FIG. 1. Bacillus, magnification 30,500 times, from tuberculous urine disclosing waxy, fatty membrane or capsule surrounding bacillus and polar bodies. Electron microscopic photographs by courtesy of Dr. Francis Bishop, Department of Physical Research, University of Rochester, N. Y.

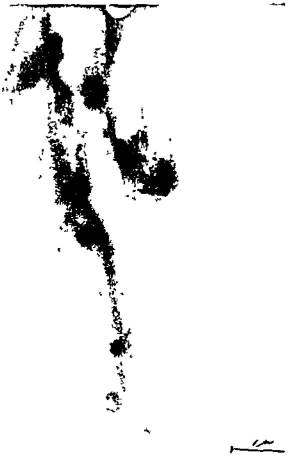


FIG. 2. Same bacillus as in figure 1 after exposure to oil for 36 hours, showing marked changes in appearance of capsule and organism proper. Electron microscopic photographs by courtesy of Dr. Francis Bishop, Department of Physical Research, University of Rochester, N. Y.

bination of streptomycin with certain other drugs in guinea pigs resulted in a greater therapeutic effect than the individual components."

Employing the hypothesis that we originally reported in December 1947, of a combination of the esters of the oil of hydnocarpus (a chaulmoogra derivative) and streptomycin on acid fast bacilli and clinical tuberculosis and based on the premise of conditioning or causing dissolution of the protecting cell wall of the tubercle bacillus with the oil enhanced the treatment (fig. 1) we are now able to report our results on in vitro studies utilized by the acid fast bacilli available; namely, the Mycobacterium of phlei, smegmatis, and tuberculosis (hominis). The only other bacillus, Hansen's bacillus (leprosy) was not studied because it does not grow in culture and can only be seen in tissue. These studies were continued utilizing several culture media: Petrognani, egg yolk, and Tween 80, and the results follow (fig. 2):

Various types of acid fast bacilli were studied for comparative purposes:

A. General method

Suspension of organisms was divided into two portions. Half was immersed in saline solution and the other half was immersed in 1:1000 solution of Moogrol in saline. Sensitivity tests to streptomycin were done upon each suspension.

1) Mycobacterium phlei. Grown in fusion broth.
   a) Saline suspension, sensitive to 0.8 micrograms of streptomycin.
   b) Moogrol suspension, sensitive to 0.4 micrograms of streptomycin.
2) Mycobacterium smegmatis. Grown in infusion broth.
   a) Saline suspension, sensitive to (but not completely inhibited by) 0.8 micrograms of streptomycin per cc.
   b) Moogrol suspension sensitive to (but not completely inhibited by) 0.4 micrograms of streptomycin per cc.
3) Mycobacterium tuberculosis.
   Grown on liquid medium containing Tween 80 and enriched with serum albumin (see below). In controls growth appeared in about 3 days and increased up to 8 days.
   a) Saline suspensions were sensitive to 3.125 units of streptomycin.
   b) Moogrol suspensions were sensitive to 1.56 units of streptomycin and growth became evident later than in a.

The strength of Moogrol used appears to delay growth of Mycobacterium tuberculosis but not to kill it.

We are able at this time to quite satisfactorily cause growth of the tubercle bacillus in from 5 to 8 days on this new clear medium, Tween 80, consisting of oleic acid and human sero-albumin. In every case the ester of hydnocarpus was used as the key for preparing the bacillus for treatment by further chemotherapeutic agents; streptomycin, the oil and diasone, the oil and para-amino-salicylic acid, diaminodiphenyl sulphone derivative of disodium formaldehyde, sulphoxalate, the oil, streptomycin and diasone. The same studies were continued in animals with the same combinations using controls in every case with each group studied with the following results.

Our clinical results are of great interest and probably are of greater appeal than the laboratory investigations, as we as clinicians in the final analysis must substantiate the findings in the test tube with the results of the individual seeking relief.

The original 6 cases have been re-examined, and while clinically the patients have remained satisfactorily well, 1 case, that of the young nurse, showed a return of the infection on culture and guinea pig inoculation. Upon repeating the same course of treatment with the addition of some doses of diasone, within 12 days the urine again became negative and has remained so to date. At the present time we have had 23 cases (table 1) under full observation and treatment; 5 are women, 18, men. The age group is of interest, all patients being in the most productive years of their life, but economic failures and liabilities because of this disease.

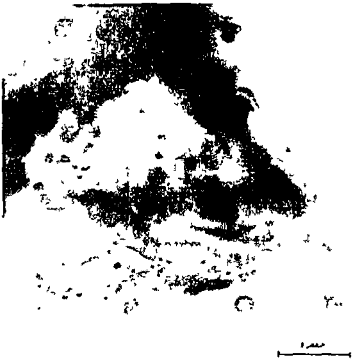


FIG. 3. Same bacillus as figure 1 after exposure to oil for 72 hours with continued changes in appearance of bacillus and practically complete disappearance of protecting membrane. Electron microscopic photographs by courtesy of Dr. Francis Bishop, Department of Physical Research, University of Rochester, N. Y.

Ten of the 23 cases had a history of urinary tuberculosis for at least 5 years; in 8 cases a nephrectomy had been done for tuberculosis and cultures still positive. Five of the patients gave a history of tuberculosis in one form or another for 10 years. Two of the patients disclosed bilateral renal tuberculosis with one functionless caseous kidney, which we treated for 6 weeks with the combined therapy, with final negative cultures from one kidney, and subsequent nephrectomy. These 2 patients were discharged from the hospital within 12 days after operation with primary healing and have remained negative as of this date.

One of the 23 patients has improved clinically in his well being, in urination, and after 17 weeks has returned to his usual occupation but we have been unable to sterilize his urine. This is the case in which the patient had undergone nephrectomy, then castration because the prostate and seminal vesicles showed

TABLE 1

CASE NO.	AGE	DURATION OF DISEASE	CHIEF SYMPTOMS	PARTS INVOLVED	TREATMENT RECEIVED PREVIOUSLY	DURATION OF PRESENT TREATMENT	TYPE OF TREATMENT RECEIVED	RESULT
	yr.	*yr.*				*days*		
1. F*	26	3	Frequency, nocturia; lost 40 lbs.	Both kidneys, bladder	None	30	Esters of chaulmoogra plus 1 gm. streptomycin daily	*Cured.* Negative urine since Apr. 1947
2. M*	39	2	Frequency, nocturia; perineal pain; left epididymitis	Left epididymis, bladder, both kidneys	None	45	Esters of chaulmoogra plus 1 gm. streptomycin daily	*Cured.* Negative urine since May 1947. Occasional pus cell
3. F*	28	$2\frac{1}{2}$	Frequency; loss of weight	Both kidneys and bladder	None	30	Esters of chaulmoogra plus 1 gm. streptomycin daily	*Cured.* Negative urine since June 1947. Reexamined Feb. '48. Negative
4. M*	22	9	Frequency, nocturia; loss of weight; draining sinus in rt. testicle	Both kidneys, rt. testicle, bladder	None	45	Right orchidectomy, ligation left vas, ester of hydnocarpus plus 1 gm. of streptomycin daily	Marked gain in weight 30 lbs., negative urine since May 1947
5. F*	30	4	Frequency, urgency	Both kidneys, bladder	Rest cure for 6 months. No improvement	35	Esters of hydnocarpus plus 1 gm. streptomycin daily	Negative for 6 mos.; bacilli then returned. Repeated course with negative urine in 15 days

6. F*	30	3	Urgency, frequency	Both kidneys, lung, bladder	Rest cure for 6 months. No improvement	35	Esters of hydnocarpus plus 1 gm. streptomycin daily	Negative urine since July 1947
7. M	41	2	Frequency; perineal pain	Prostate, seminal vesicles, bladder	None	30	Esters of hydnocarpus plus 1 gm. streptomycin daily	*Cured.* Negative urine since Jan. 1948
8. M	37	9	Frequency, hematuria, nocturia; draining sinus in lung	Old tuberculous lung with sinus, bladder, prostate, both kidneys	Sanatorial only, with phrenictomy and pneumothorax	45	Esters of hydnocarpus plus 1 gm. streptomycin daily	Pulmonary sinus permanently closed in 21 days. Urine negative since Jan. 1948
			Frequency, nocturia; loss of 30 lbs. weight	Both kidneys, bladder, prostate	Sanatorial care 2 yrs. L. nephrectomy 3 yrs. ago	30	Esters of hydnocarpus plus 1 gm. streptomycin	*Cured.* Completely negative urine since Feb. 1948
10. M	42	6	Frequency, nocturia, hematuria	Remaining left kidney, prostate, bladder	Rt. kidney removed 2 yrs. ago	35	Esters of hydnocarpus plus 1 gm. streptomycin daily	*Cured.* Negative urine since Feb. 1948
11. M	40	10	Frequency, nocturia, hematuria; loss of weight; Daily rise in temp.	Both kidneys, rt. caseous, functionless	None	30 days preparatory to surgery	Esters of hydnocarpus plus 1 gm. streptomycin plus 1 gm. diasone daily	*Cured.* Negative urine since Mar. 1948
12. M	36	11	Frequency, nocturia	Rt. kidney, bladder, prostate, seminal vesicles	Left nephrectomy 9 years ago	45	Esters of hydnocarpus 1 cc. daily. ½ gm. streptomycin. 1 gm. diasone daily	Clinically better. Urine persistently positive for bacilli. Our one failure.

TABLE 1—*Continued*

CASE NO.	AGE	DURATION OF DISEASE	CHIEF SYMPTOMS	PARTS INVOLVED	TREATMENT RECEIVED PREVIOUSLY	DURATION OF PRESENT TREATMENT	TYPE OF TREATMENT RECEIVED	RESULT
	yr.	*yr.*				*days*		
13. F	28	2	Frequency, hematuria; cough; loss of weight; positive sputum	Both kidneys, bladder, both lungs peppered	100 gm. streptomycin previously administered without results	35 days preparatory to surgery with negative sputum and urines 21 days	Esters of hydnocarpus 2 cc daily, ½ gm. streptomycin 1 gm. diasone daily	*Cured.* Negative urine since Apr. 1948
14. M	36	11	Frequency, nocturia, hematuria	Remaining left kidney, bladder, left epididymis	Rt. nephrectomy 8 years ago. Continuous positive urine	30	Esters of hydnocarpus 1 cc, 1 gm. streptomycin, 1 gm. diasone daily	*Cured.* Negative urine since Apr. 1948
15. M	41	20	Frequency, pain in scrotum; progressive loss in weight	Old pulmonary lesion with draining sinus. Genital tuberculosis involving prostate, seminal vesicles and both epididymes with draining sinuses from latter.	In sanatorium for past 12 yrs. rest cure	45	Esters of hydnocarpus 2 cc, ½ gm. streptomycin and 1 gm. diasone daily	Negative sputum. Negative urine. Healed epididymis since Apr. 1948
16. M	37	2	Cough, pain in right epididymis; draining rectal sinus	Rt. epididymis, lung, anorectal fistula	Sanatorial rest	40	Esters of chaulmoogra plus 1 gm. streptomycin daily	Sinus closed. Draining epididymis closed, cough disappeared. Sputum negative. Urine negative as of 4/1/48

disease with streptomycin in combination with the oil rather than as an individual component. The term of treatment depends upon the results. It is of great interest to note that with the one exception the urine was sterilized within 20 to 25 days, but treatment was continued for an additional 4 to 6 weeks as a precautionary measure.

The use of diasone in addition to streptomycin appears to be a distinct step forward and is part of the treatment which should be instituted somewhere along the course. In no cases have there been any toxic reaction, or systemic changes, as noted with streptomycin alone. Only 1 patient disclosed a mild tinnitus which disappeared promptly after the cessation of treatment.

This method of treatment, as originally stated, is not recommended to supplant surgery. The degenerated, functionless, caseous kidney or testicle is still a surgical entity and should be removed, but the results that we have obtained, and also others, warrant the institution of this treatment as a preliminary measure before surgery, after surgery, and in also those cases in which surgery is not indicated or is impossible because of bilateral involvement without too much damage.

Medical Center Bldg., Buffalo, N. Y.

REFERENCES

Calloman, F. T., Kolmer, J. A., Rule, A. M. and Paul, A. J. Proc. Soc. Exp. Biol. & Med., 63: 237, 1946.
Lincoln, E. M., Kirmse, T. W. and Devito, E.: J.A.M.A., 136: 593, 1948.
Petter, C. K. and Prenzlau, W. S.: Ill. Med. J., 85: 188, 1944.
Slotkin, G. E.: J. Urol., 58: 464, 1947.
Smith, M. I., McClosky, W. T. and Emmart, E. W.: Proc. Soc. Exper. Biol. & Med., 62: 157, 1946.
Waksman, S. A.: J.A.M.A., 135: 478, 1947.
Wilbolz, H.: J. Urol., 21: 145, 1929.

THE JOURNAL OF UROLOGY
Vol. 61, No. 3, March 1949
Printed in U.S.A.

DISCUSSION

DR. ELMER HESS (Erie, Pa.): I have followed this work of Dr. Slotkin's with a great deal of curious interest. After his remarkable report last year, the treatment advocated by him and his fellow research workers was applied to our patients suffering with urogenital tuberculosis. We even took the trouble to send for our old cases and asked them to return for evaluation of their present condition, with the thought that some of them might be helped.

We had a number of nephrectomized patients who were found to still have bacilli in their urine, with continuing subjective symptoms. Several of these have become clinically relieved both of their symptoms and of the organisms in their urine. They have been able at least temporarily to resume an efficient economic and social life. Others have gone along for a few months with improvement, only to become incapacitated later. These should, I believe, undergo a second course of therapy.

We have seen some inoperable cases of urological tuberculosis become operable after the therapy. We are now putting all patients with urological tuberculosis on the therapy as part of any contemplated surgical procedure for the disease, operating at the end of the second week and continuing the routine treatment through the postoperative and convalescent periods.

A word of warning: The treatment is not without danger. We lost a patient from an uncontrollable exfoliative dermatitis. This was due to inexperience. When the dermatitis first appeared, the treatment was stopped, with abatement of the dermatitis. The therapy was resumed too soon, and a second, fatal, dermatitis ensued. If the treatment is discontinued because of complications, it should not be resumed for a long period of time and then should be most carefully observed if repeated, and discontinued very promptly and completely discarded if any subsequent reaction takes place.

Another word of warning: Do not consider this a cure. Time alone will prove its value. At present it appears to have promise.

In conclusion, tuberculosis is a general disease, and should be managed by others than the urologist. Our role is that of a consultant when the disease invades the urinary pathways, and our treatment is only a phase in the overall management of the case.

DR. HERBERT B. WRIGHT (Cleveland, Ohio): I trust that the evidence presented has aroused enough interest in Dr. Slotkin's method of treating urinary tract tuberculosis to cause its use to become progressively more widespread. Even though the percentage of cures is undetermined as yet, the cessation of urinary symptoms in patients thus treated is striking. The relief afforded the patient with a contracted tuberculous bladder is really remarkable.

Two observations made in our small series may be of interest:

The preparation of chalmoogra oil esters comes in a bottle with a top which screws on, and has no rubber diaphragm or other type of modern sterile packaging. This caused us some worry regarding the sterility of the preparation. On investigation, however, the possibility of this oily solution, containing 4 per cent

BRANCH SOCIETIES OF THE AMERICAN UROLOGICAL ASSOCIATION

CHICAGO BRANCH

President—DR. JAMES W. MERRICKS, 104 S. Michigan Ave., Chicago, Illinois
Vice-President—DR. JAMES I. FARRELL, 636 Church St., Evanston, Illinois
Secretary-Treasurer—DR. J. S. GROVE, 185 N. Wabash Avenue, Chicago 2, Illinois
Executive Committee—DR. R. H. HERBST, 104 S. Michigan Ave., Chicago 3, Ill.; DR. W. J. BAKER, 7 W. Madison St., Chicago, Ill.; DR. N. J. HECKEL, 122 S. Michigan Ave., Chicago 3, Ill.; DR. R. D. HERROLD, 6 N. Michigan Ave., Chicago 3, Ill.; DR. I. J. SHAPIRO, 185 N. Wabash Ave., Chicago, Ill.

DETROIT BRANCH

President—DR. GEORGE E. CHITTENDEN, 7815 E. Jefferson, Detroit, 14, Michigan
President-elect—DR. CARLISLE F. SCHROEDER, 7815 E. Jefferson, Detroit, 14, Michigan
Secretary-Treasurer—DR. WILLIAM BROMME, 10 Peterboro Street, Detroit, Michigan
Executive Committee—DR. HAZEN MILLER, Washington Square Building, Royal Oak, Michigan; DR. ORMOND S. CULP, Henry Ford Hospital, Detroit, Michigan; DR. ROBERT A. BURHANS, 806 Olds Tower Bldg., Lansing, Michigan

PHILADELPHIA BRANCH

President—DR. BOLAND HUGHES, Medical Arts Bldg., 16th and Walnut Sts., Philadelphia, Pa.
Vice-President—DR. WALTER W. BAKER, 255 S. 17th St., Philadelphia, Pa.
Secretary-Treasurer—DR. GEORGE D. SHOUP, 121 W. Walnut Lane, Philadelphia, Pa.
Executive Committee—DR. EDWARD CAMPBELL, Medical Arts Bldg., 16th and Walnut Sts., Philadelphia, Pa.; DR. THEODORE R. FETTER, 255 S. 17th St., Philadelphia, Pa.; DR. LLOYD B. GREENE, Medical Arts Bldg., 16th and Walnut Sts., Philadelphia, Pa.; DR. PAUL R. LEBERMAN, Medical Arts Bldg., 16th and Walnut Sts., Philadelphia, Pa., DR. CHARLES A. W. UHLE, 255 S. 17th St., Philadelphia, Pa.

PITTSBURGH BRANCH

President—DR. HOLISTER W. LYON, Spirit Bldg., Punxsutawney, Pa.
Vice-President—DR. WILLIAM W. WIGHTMAN, 917 Highland Bldg, Pittsburgh, Pa.
Secretary-Treasurer—DR JOHN L. HAMILTON, 7086 Jenkins Arcade, Pittsburgh, Pa.
Executive Committee—DR. BENJAMIN LEVENT, 422 Jenkins Arcade, Pittsburgh, Pa.; DR. [illegible]

ST. LOUIS BRANCH

President—DR. ELMER E. SEXTON, Paul Brown Bldg., St. Louis, Mo.
President-Elect—DR. JOHN F. PATTON, University Club Bldg., St. Louis, Mo.
Secretary-Treasurer—DR. CARL A. WATTENBERG, Beaumont Medical Bldg, St. Louis, Mo.
Executive Committee—DR. JOHN F. PATTON, St. Louis; DR. H. H. KRAMOLOWSKY, St. Louis; DR. STEPHEN TAPPER, St. Louis; and the officers ex officio.